



Historical Vignette

The history of surgery in disorders of sexual development

Cenk Buyukunal ^{a,*}, Kristen A. Zeller ^b, Senol Emre ^c, Don K. Nakayama ^d^a Division of Pediatric Urology, Department of Pediatric Surgery, Cerrahpasa Medical Faculty, Istanbul University-Cerrahpasa, 34301 Cerrahpasa, Istanbul, Turkey^b Wake Forest University School of Medicine, Winston-Salem, NC^c Istanbul University-Cerrahpasa, Department of Pediatric Surgery, Cerrahpasa Medical Faculty, 34301 Cerrahpasa, Istanbul, Turkey^d University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, NC

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ABSTRACT

Disorders of sexual development (DSD) have been documented throughout human history with fascination. Healers of all cultures have struggled to explain, and later correct with surgery, the physical manifestations of DSD. DSD was portrayed in the mythology, legends, and art of the ancient Greeks, Romans, Sumerians, Babylonians, and Egyptians.

Techniques of feminizing genitoplasties date to the time of Celsus in the time of Christ. Acceptable operative therapy for feminine phenotypes of DSD came in the 19th and 20th centuries. Masculinizing procedures, inherently more complex than feminizing genitoplasties, initially were variations of procedures for severe forms of hypospadias. Today most total penile reconstruction procedures use reconstructive and microvascular techniques invented in 20th century.

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1. Ancient History

Problems related to disorders of sex development (DSD) include anomalies of sex chromosomes and biochemical pathways that result in a broad range of physical manifestations involving the gonads and internal and external genitalia. Throughout history, humankind has recorded with fascination, struggled to explain, and later correct with surgery, the physical manifestations of DSD.

1.1. Mythology and portrayals in art

Clay tablets from 4000 to 5000 BCE record the Sumerian creation myth of Enki and Ninnah, tales that include how DSD anomalies came about [1]. Enki was the god of the soil or earth, whose home was the underground sweet waters of Mesopotamia. As the deity associated with fertility and irrigation, he was depicted as having an insatiable sexual appetite. He and the goddess Ninnah became drunk at a banquet of the gods and started a contest where Enki created humans with defects that Ninnah would counteract, such as a being that was unable to talk nor feed itself. Among them was a hermaphrodite [2].

* Corresponding author. Tel.: +9 053 2212 1213.

E-mail address: buyukunal@gmail.com (C. Buyukunal).

The Babylonians (CA 2300–539 BCE) and the Phoenicians (1550–300 BCE) documented hermaphroditism centuries before the Ancient Greeks (12th–9th centuries BCE–600 CE) [3]. In ancient Greek and Roman mythology, Hermaphroditos has the body of a small-breasted woman and male genitalia. In one account of how he assumed his bodily form, he was the beautiful son of his handsome father Hermes and his lovely mother Aphrodite. A nymph, Salmacis, spied him while he was bathing in her pool near Halicarnassus, a Greek town now on the southwestern coast of Turkey. She immediately fell in love with him and embraced him. As she held him, she asked the gods never to separate the two lovers. Her wish was granted, and the result was a beautiful youth with the breasts of a woman and the genitals of a man [2,4].

Hermaphroditos was celebrated in Greek and Roman statuary. A full-sized standing figure from Pergamon dates from the 3rd century BCE. Now in the Istanbul Archeological Museums, the bisexual nature of Hermaphroditos is discrete, with a torso of a young man, but with small but well-shaped breasts with enlarged nipples and modest male genitalia (Fig. 1) [5]. The Sleeping Hermaphroditos from the 2nd century BCE is one of the best-known renditions, with copies on display at the Louvre, the Galleria Borghese, and Palazzo Massimo Alle Terme. The languid figure is entirely female except for the genitals, which are male (Fig. 2) [6].

One of the most explicit statues of Hermaphroditos, the so-called Hermaphroditos of Mirecourt (it was actually discovered in 1831 in Saxon-Sion), is on display in the Musée Départemental d'art Ancien et Contemporain in Epinal, France. The figure has a feminine body with

immature breast development and a diminutive but erect penis with hypospadias. It is thought to be a copy of a figure from the 2nd or 1st century BCE [7,8].

During the Ancient Rome (753 BCE–476 CE), hermaphrodites were among the infants with congenital malformations that were abandoned on an island in the Tiber to die or killed immediately [9,10]. One who survived into adulthood was Favorinus of Arelate (CA 80–160 CE), a Roman philosopher, who was described by a contemporary as beardless, with a high-pitched voice, and “a eunuch born without testicles.” [11]

1.2. Primitive operations

Castration and penectomy is as old as civilization. The Code of the Babylonian king Hammurabi (2123–2081 BCE) specifies castration as a punishment for sexual crimes [12,13]. During the 20th dynasty in Egypt (1200–1085 BCE), castration and penectomy were methods of punishment for adult males, particularly the soldiers of defeated enemies. Pharaoh Merneptah (1212–1203 BCE) ordered the amputation of the phalluses of 6365 Libyan invaders, an event memorialized on the walls of the Karnak Temple near Luxor in Egypt [14].

In South Asia, the Hijra, or “third sex,” have undergone a ritual demasculinization in boyhood, with removal of the penis, testes, and scrotum, as a sacrifice to receive a spiritual prowess [15]. The development of secondary sexual characteristics is thus prevented, and the Hijra maintains a childlike appearance [16].

2. Classical Rome and Middle East

Aulus Cornelius Celsus (25 BCE–50 CE), the Roman encyclopedist whose extant medical volumes formed *De Medicina*, was the first to document congenital vaginal abnormalities. He described an incision for the surgical treatment of imperforate hymen or transverse vaginal septum. In higher and more severe forms, after the incision he described using tampons or metallic sounds with some cicatrizing creams and ointments to prevent adhesion formation in the neovagina [17].

Historian Gregory Tsoucalas at the Democritus University of Thrace discovered passages describing intersex operations in “Library of World History,” a lengthy treatise written sometime between 80 and 20 BCE by the Greek historian Diodorus Siculus. One was a young woman whose sole perineal opening was a fistula behind the pubis. The area swelled into a painful tumor, which a pharmacist lanced, releasing a pair of testes and a phallus. Somehow he probed the glans to create a passage into the urethra, which he held open with a silver catheter. He scarified the area and drew the passage closed around the catheter. The pharmacist, wrote Tsoucalas, “demanded a double fee, as he undertook a case of a sick female and delivered a cured young male.” [11]

The Alexandrian physician and surgeon Paulus Aegineta (625–690), in his *Epitomae Medicae Libri Septem*, recorded forms of DSD. He described female and male as well as a third type in males with perineal hypospadias, which he classified as an incurable form [18]. His text had wide influence and was the principal source for Abucasis of Cordoba (936–1013) and Avicenna in Persia (980–1037), surgeons who epitomized the Islamic Golden Age [19]. In addition to his description of castration, Albucasis documented observations about hermaphroditism and its treatment [20].

Şerafeddin Sabuncuoğlu (1385–1468), a 15th century surgeon from central Anatolia, wrote one of the earliest definitive texts on the anatomy and surgical treatment of hermaphroditism. In his three-volume manuscript, he devoted a chapter to the genital abnormalities of children. Various techniques for castration and cliterectomy were depicted in vivid pictures in color. One patient appeared to have clitoromegaly from adrenogenital syndrome. Fused labia minora were also illustrated. Of note, female surgeons (*tabibe*) routinely performed surgery for such gynecological procedures involving the female genitalia, an interesting medical and social development for the 15th century. Sabuncuoğlu's

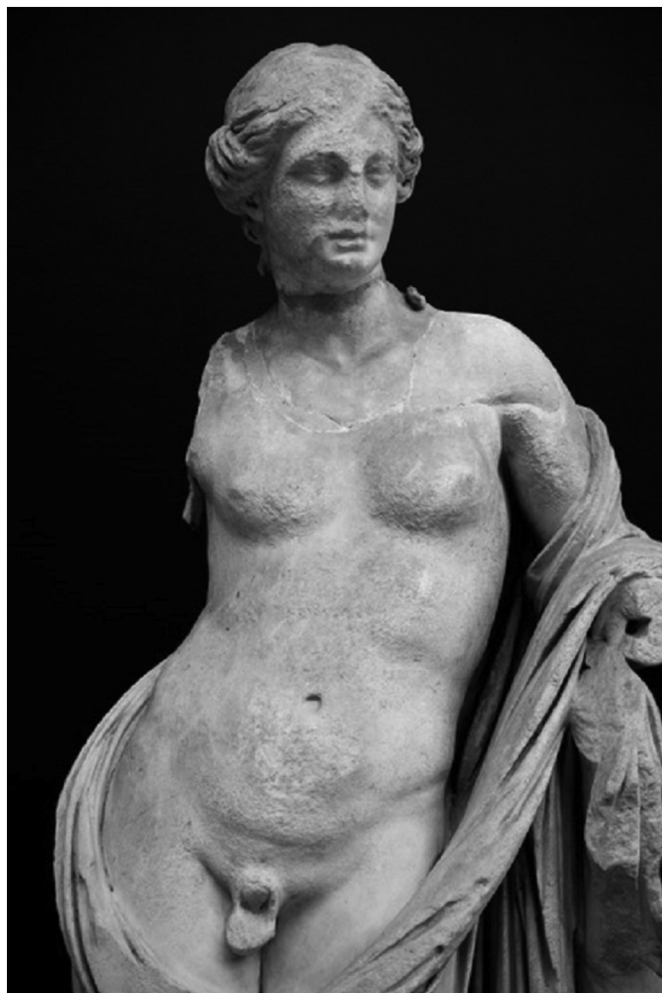


Fig. 1. Statue of Hermaphroditos from Pergamon, 3rd century BCE. Istanbul Archeological Museum.



Fig. 2. Sleeping Hermaphroditus, 1st century BCE. Werner Forman Archive, N. J. Saunders, National Museum, Rome.

text has a number of illustrations of *tabibe* holding scalpels performing surgical operations on the perineum [20–24].

3. Early Modern Era

In the mid 16th century, Ambroise Paré (1510–1590) in Paris described hermaphroditism in detail and depicted informative illustrations in his manuscript. He fashioned an artificial penis using a wooden pipe that allowed urination in a man who had sustained a traumatic amputation [25,26]. In Italy the anatomist and surgeon Hieronymus Fabricius d’Aquapendente (1533–1619) wrote on vaginal atresia, imperforate hymen and hermaphroditism. In addition to his writings, he performed surgical treatment for two women with vaginal atresia [27].

In his highly influential textbook of surgery, *Cours d’opérations de chirurgie démontrées au Jardin du Roi* (A Course of Surgical Operations Demonstrated in the Royal Garden, 1707), Pierre Dionis (1643–1718) in Paris attributed lesbian behavior to an enlarged clitoris. He described a special technique for clitoridectomy based on his measurements of what he considered a normal and an abnormally enlarged clitoris [28].

4. Contemporary Concepts

In her article on the contemporary history of genital reconstruction, Justine Schober of Erie, PA, presented the step-wise description of how the operations for feminizing and masculinizing genital reconstruction evolved into today’s concepts for the surgical management of DSD [29]. A summary of some of the surgical highlights from her article follows.

4.1. Feminizing genital reconstruction

- The goals for feminizing genital reconstruction for DSD are threefold:
- reduction of the erectile part of the enlarged phallus with preservation of the neurovascular bundle and glanular tissue,
 - creation of a normal looking vaginal introitus (labia majora and minora), and
 - construction of a neovagina with normal depth and diameter.

The first reconstructive priority recognized by surgeons was the creation of a vagina suitable for intercourse. Guillaume Dupuytren (1777–1835) made the first attempt to reconstruct a neovagina for vaginal atresia in 1817 [30]. He created a vaginal tract by forming a perineal space between the bladder and rectum. Without a skin graft or a mold to keep the space open, the procedure was unsuccessful [31].

Nearly contemporaneously in 1818, on the other side of the Atlantic, John Syng Dorsey (1783–1818) of Philadelphia, described two operations for membranous obstruction and a high septal obstruction for imperforate vagina, reminiscent of the writings of Celsus nearly two

millennia previously. He used a cruciate incision to create a defect between the bladder and rectum, and introduction of a sponge for the prevention of adhesions. His uncle and mentor, Philip Syng Physick (1768–1837), used his nephew’s technique for a high-type vaginal atresia using Dorsey’s technique, including the use of sponges in the defect to keep the defect from closing [32].

Skin grafts were a logical step to provide a skin-lined neovagina that remained open. After creating an opening with an “H”-shaped incision, Heppner used skin flaps from the proximal thigh to give the sides of the defect a lining of skin in 1870 [33]. In 1898 Abbe, MacIndoe, and Bannister used split-thickness skin grafts [34,35]. In the 20th century, the development of new techniques such as tissue expansion and fasciocutaneous flaps provided additional options for vaginal reconstruction, including the use of segments of intestine and the sigmoid colon [29].

Early operations for the enlarged clitoris were designed to hide the structure, bury most of its length, or reduce it in size by excising a segment and reconstructing the remainder [29]. (Tables 1,2,3,4).

4.2. Masculinizing procedures

The goals for masculinization procedures focus on genitoplasties that are not much different than those for severe hypospadias. The main

Table 1
Perineal operations to create a neovagina.

Year	Author(s) and reference	Description
1817	Dupuytren ^{36–38}	Surgery for vaginal atresia by creating a perineal defect.
1818	Dorsey [19]	Cruciate incision for membranous obstruction of frhe vagina and high vaginal septum; introduction of a sponge to prevent adhesions.
	Physick ¹⁹	Dorsey’s technique for high vaginal atresia, with insertion of sponges to prevent premature closure and adhesion formation.
1870	Heppner ²¹	“H”-shaped incision of the rectovaginal septum and flaps from the proximal thigh to create a neovagina.
1898	Abbe, MacIndoe, and Bannister ^{41, 42}	Mold covered by a split-thickness skin graft.
1936	Monod and Iselin ²⁰	Modification of Dupuytren’s technique, with split-thickness skin grafts over a stent to create a skin-lined neovagina.
1938	Wharton ³⁹	Creation of a vaginal pouch, with molds to shape it into a neovagina over 6 months.
1948	Counselor ⁴⁰	Perineal pouch with enlargement by molds.
1994	Jackson and Rosenblatt ⁴³	Mold covered by an absorbable adhesion barrier.
1997	Peña ^{44–46}	Total urogenital mobilization for cloacal malformations; later application to urogenital sinus anomalies.

Table 2
Vaginoplasty operations using skin flaps.

Year	Author(s) and reference	Description
1989	Wee and Joseph ⁴⁸	Neovagina using a pudendal thigh fasciocutaneous flaps.
1989	Passerini-Glazel ³²	Inversion of skin of urogenital sinus and anastomosed to vaginal opening, phallic skin used to create labia, inverted “U”-flap for introitus.
1991	Johnson ⁵¹	Tissue expanders in labia to create skin for vaginal reconstruction
1992	Dumanian and Donahoe ⁵⁰	Rotational buttock flaps for inadequate perineal skin.
1994	Gleson ⁴⁹	Neovagina using a pudendal thigh fasciocutaneous flaps.

Table 3
Other methods for vaginoplasty.

Year	Author(s) and reference	Description
1904	Baldwin ⁵³	Use of a segment of intestine.
1911	Schubert ³⁸	Use of sigmoid colon.
1952	Schmid ³⁸	Use of sigmoid colon.
1960	Pratt ⁵⁶	Use of sigmoid colon.
1969	Davyof ⁵⁴	Cylinder-shaped graft of peritoneum created a space between the bladder and rectum from the abdomen; graft sutured to the vulva from the perineum.
1986	Ashworth ⁵³	Used amnion over a mold to construct a vagina.
1994	Hendren and Atala ⁵⁷	Perineal pullthrough for high urogenital sinus.

steps are:

- repair of hypospadias,
- correction of scrotal abnormalities,
- excision of Müllerian duct structures, and
- excision of atypic gonadal tissues.

Reconstruction of an amputated penis required the development of transfer of vascularized skin flaps during the 20th century, beginning with the tube pedicle flap by Sir Harold Gilles during the World War I [36]. In 1936, Nikolai Borgoras, a Russian surgeon, used a tubularized pedicle flap for total penile reconstruction [37]. In 1946, Gillies and Maxwell Maltz used a tube as a urethra and placed it in another tube from the abdomen, a “tube in tube” modification. As an added feature, they also used a piece of cartilage from a rib as a stiffener [38].

Penile reconstruction procedures have evolved in parallel with advancements in plastic surgical techniques and experience in microsurgery. The complexity and technical challenge of penile reconstruction underscore the need for a multidisciplinary approach involving reconstructive plastic surgeons and pediatric urologists. Additionally, psychological support before and after the operation by a pediatric psychiatrist is necessary for a satisfactory result [29]. (Table 5).

4.3. Internal genitourinary anatomy

As modern research defined the pathological and endocrinological foundations of DSD, the surgical assessment of internal genitourinary anatomy and gonadal histopathology became necessary to define the condition and its prognosis. Minimally invasive surgical procedures (MIS), both with standard laparoscopy and robotic technology, have allowed diagnostic assessment with minimal impact to the patient [39–41].

The aims of internal genitourinary assessment are:

- ovotesticular DSD require accurate gonadal assesment and biopsy,
- removal of gonads with high potential for malignancy, and
- removal of Müllerian remnants that cause recurrent infections.

Table 4
Operations for clitoral enlargement.

Year	Author(s) and reference	Description
1939	Ombredanne [5]	Skin flap coverage of the clitoris.
1957	Stefan and Pinsker ²⁵	Suture obliteration of the corpora with preservation of neurovascular supply, reduction of the glans circumferentially, subcutaneous burial of the glans.
1961	Lattimer ²⁶	Clitoris is entirely preserved and submerged, reduction of glans by trimming its corona.
1965	Pellerin ²⁷	Relocation of the corpora deep and inferior to the pubic symphysis.
1970	Randolph and Hung ²⁸	Relocation of the clitoris beneath the symphysis and suturing it to the periosteum.
1973	Spence and Allen [29]	Excision of the shaft while preserving the glans, fixation of the glans to the pubis.
1974	Kumar ³⁰	Partial excision of the corpora, reduction of the dorsum of the glans, suture of ventral remnant to the stump of the corpora.
1983	Kogan ³¹	Open the tunica albuginea, excise erectile tissue by proximal and distal suture ligation, wedge reduction of the glans.
1989	Passerini-Glazel ³²	Partial excision of the crura, reduction and relocation of the glans under re-modeled labia minora, urethral flap to create a mucosal cover under the clitoris.
1991	Hutson ³⁴	Excision of erectile tissues from the ventral surface, folding of clitoris and suturing it along axis, clitoral skin used to create labia minora.
1993	Sagehashi ³³	Preservation of the entire corporal tissue and glans with the neurovascular bundle intact, suture of the glans to the pubis.

Table 5
Pedicled flaps for penile reconstruction.

Year	Author(s) and Reference	Description
1956	Morales, O'Connor, and Hotchkiss ⁵⁷	A single tubed skin flap technique by using groin flaps
1964	Snyder ⁶⁴	Single pedicled infraumbilical flap technique with skin lined conduit for urethral formation
1978	Puckett and Montie ⁶⁶	First description of a pedicled groin flap. A rigidity prosthesis was also used. A rectus abdominis muscle flap was used to cover the prosthesis and whole organ is covered by bilateral pedicled groin flaps
1982	Song ⁶⁵	Infraumbilical midline pedicled flap nourished from superficial epigastric vassels. Urethra was reconstructed from scrotal or abdominal flap
1983	Persky, Resnick, and Desprez ⁶⁸	Penile reconstruction with gracilis pedicle grafts
	Dias (1984), ⁶² Patil, Dias, and Thatte (1987) ⁶³	SEPA (Superficial External Pudendal Artery) flap technique: A bipedicled infraumbilical skin flap-an infraumbilical abdominal skin flap and a skin graft are wrapped for the formation of phallus and urethra
1992	Sadove and McRoberts ⁷⁰	First description of free osteocutaneous fibular flap for total penile reconstruction
2000	Santanelli and Scuderi ⁶⁹	Penile reconstruction by using neurovascular tensor facia lata island flap
2005	Bettocchi, Ralph, and Pryor ⁷⁴	Pedicled suprapubic abdominal wall flap for phalloplasty
	Mutaf (2006), ⁷¹ Rubino (2009), ⁷² Lee (2009) ⁷³	Pedicled anterolateral thigh flap (ALT) technique for reconstruction
2006	Hu, Lu, Zhang, et al. (2006) ⁷⁷	Report of an isolated case of penile allotransplantation
2006	Djordjevic, Bumbasirevic, Vukovic, et al. ⁷⁵	Musculocutaneous latissimus dorsi free transfer flap for phalloplasty
2006	Lin and Chen ⁷⁶	Free thoracodorsal artery perforator flap for penile reconstruction

5. Conclusion

The history of surgery for DSD parallels the entire span of human civilization, from genital mutilation to present-day techniques for female

and male reconstruction. With each advance in plastic and reconstructive surgery comes new refinement with the potential for better cosmetic and functional outcomes for these challenging patients. MIS and robotic surgery are also being employed to assess and reconstruct anatomical malformations and remove premalignant gonads.

During the last 30 years the reality that “performing good surgery is not sufficient” is increasingly recognized by patients and parents. Super-seding the technical success of an operation, success in psychosocial adjustment should be the primary goal for decisions regarding sexual assignment and genitoplasty.

Long-term results of the psychosocial outcomes will give us the best information to determine if we, as surgeons, are successful in the treatment of DSD patients. The formation of DSD councils in specialized clinics is extremely important. Especially helpful are intersex support groups and other patient and parent advocacy groups. It is important to connect patients and parents with effective psychosocial support groups.

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