EXSTROPHY EPISPADIAS

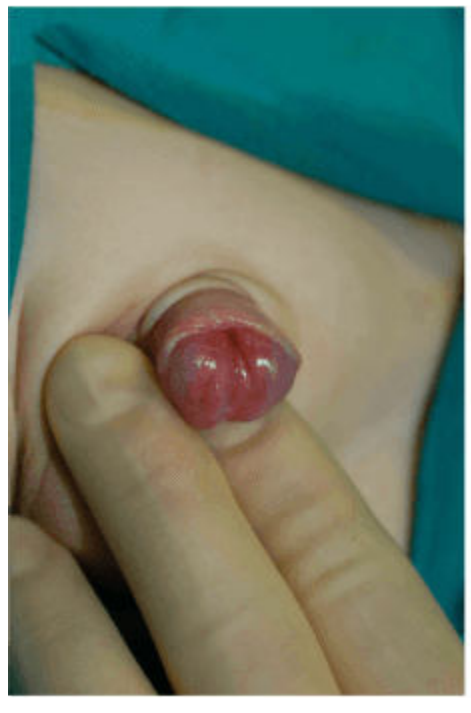
Introduction

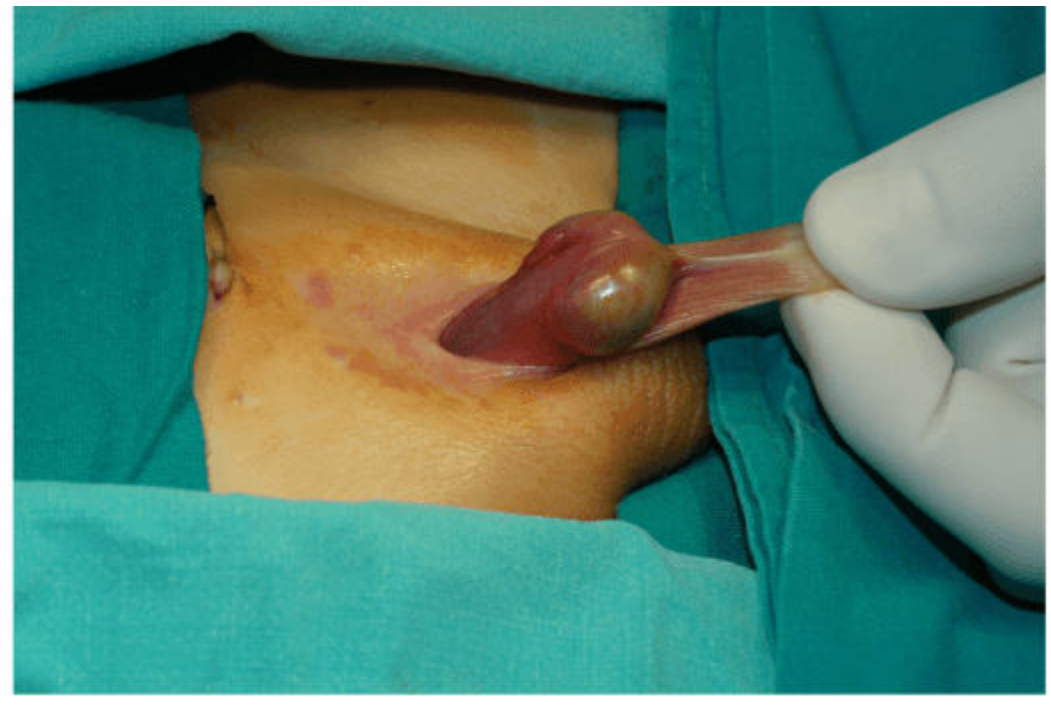
Bladder exstrophy is a rare midline defect and exists as part of a larger spectrum of abdominal-pelvic fusion abnormalities, known collectively as the exstrophy-epispadias complex (EEC).

Presentation of EEC can range from isolated glanular epispadias to cloacal exstrophy, in which several other organ systems may be affected.

Spectrum

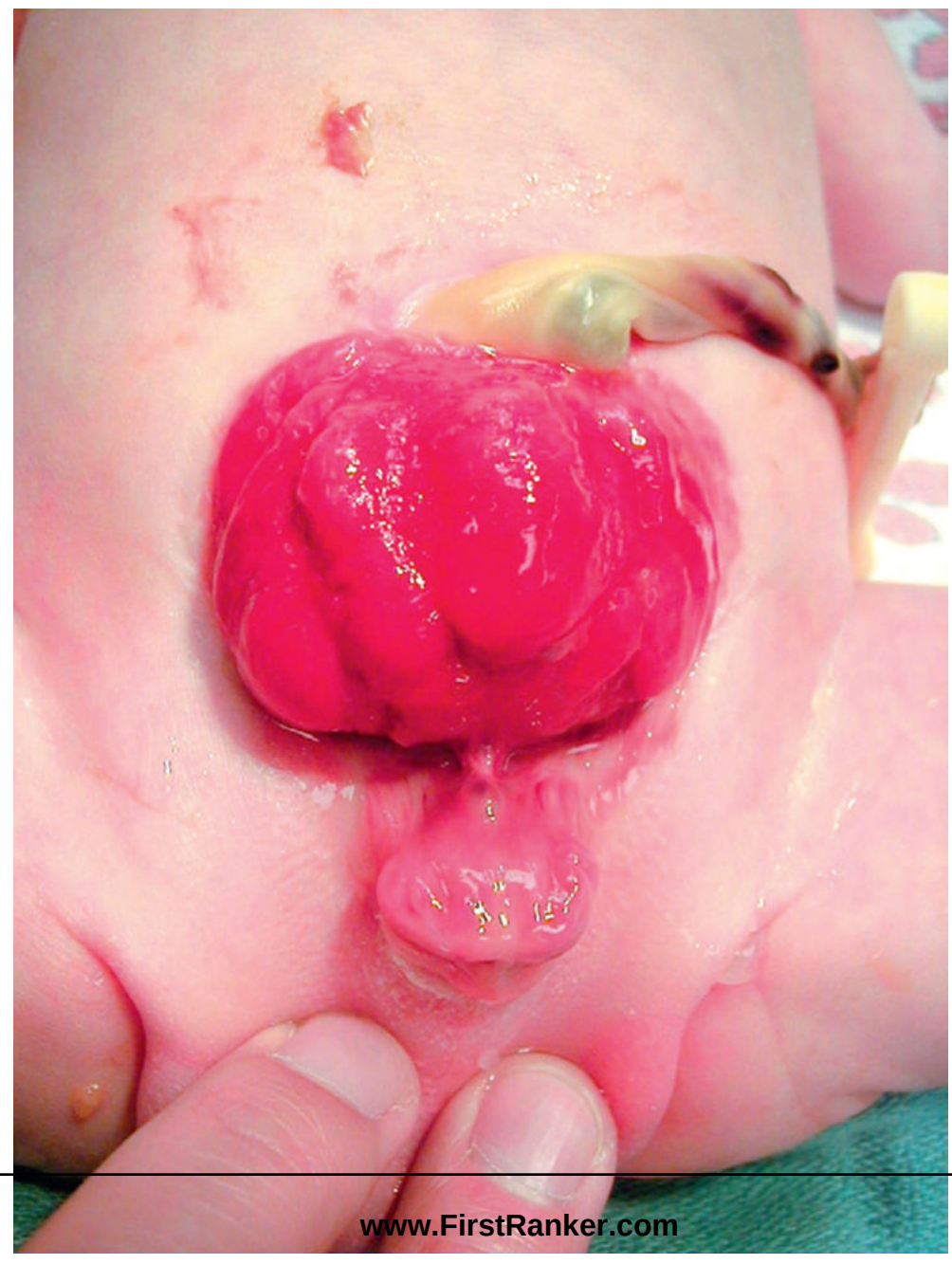
Epispadias	the urethra is a partial or complete open plate on the dorsal surface of the phallus.
Classic bladder exstrophy	the bladder is an open plate on the low abdominal wall and the urethra is epispadic.
Cloacal exstrophy	the bladder and the ileocecal junction of the bowel are an open plate on the low abdominal wall associated with other malformations.
Exstrophy variants	partial manifestations are seen of the above malformations.





Anatomic pathology: Bladder exstrophy

- Brock and O'Neill described exstrophy as
  - 'if one blade of a pair of scissors were passed through the urethra of a normal person; the other blade were used to cut through the skin, abdominal wall, anterior wall of the bladder and urethra, and the symphysis pubis; and the cut edges were then folded laterally as if the pages of a book were being opened.'



- Presence of a layer of urothelium on the anterior abdominal wall representing the bladder and urethra.
  - At birth, the urothelium is usually normal in appearance.
  - Ectopic bowel mucosa or polypoid lesions consistent with cystitis cystica and/or glandularis may be present.
  - If left untreated and without meticulous protection after birth, the exposed urothelium will undergo squamous metaplasia in response to acute and chronic inflammation. Other inflammatory changes such as cystitis cystica and/or glandularis will also be seen.
  - When left chronically exposed to the environment, the areas of squamous metaplasia often undergo malignant degeneration to adenocarcinoma or squamous cell carcinoma.

Associated anomalies

- Classic exstrophy and epispadias have a relatively low incidence of associated anomalies.

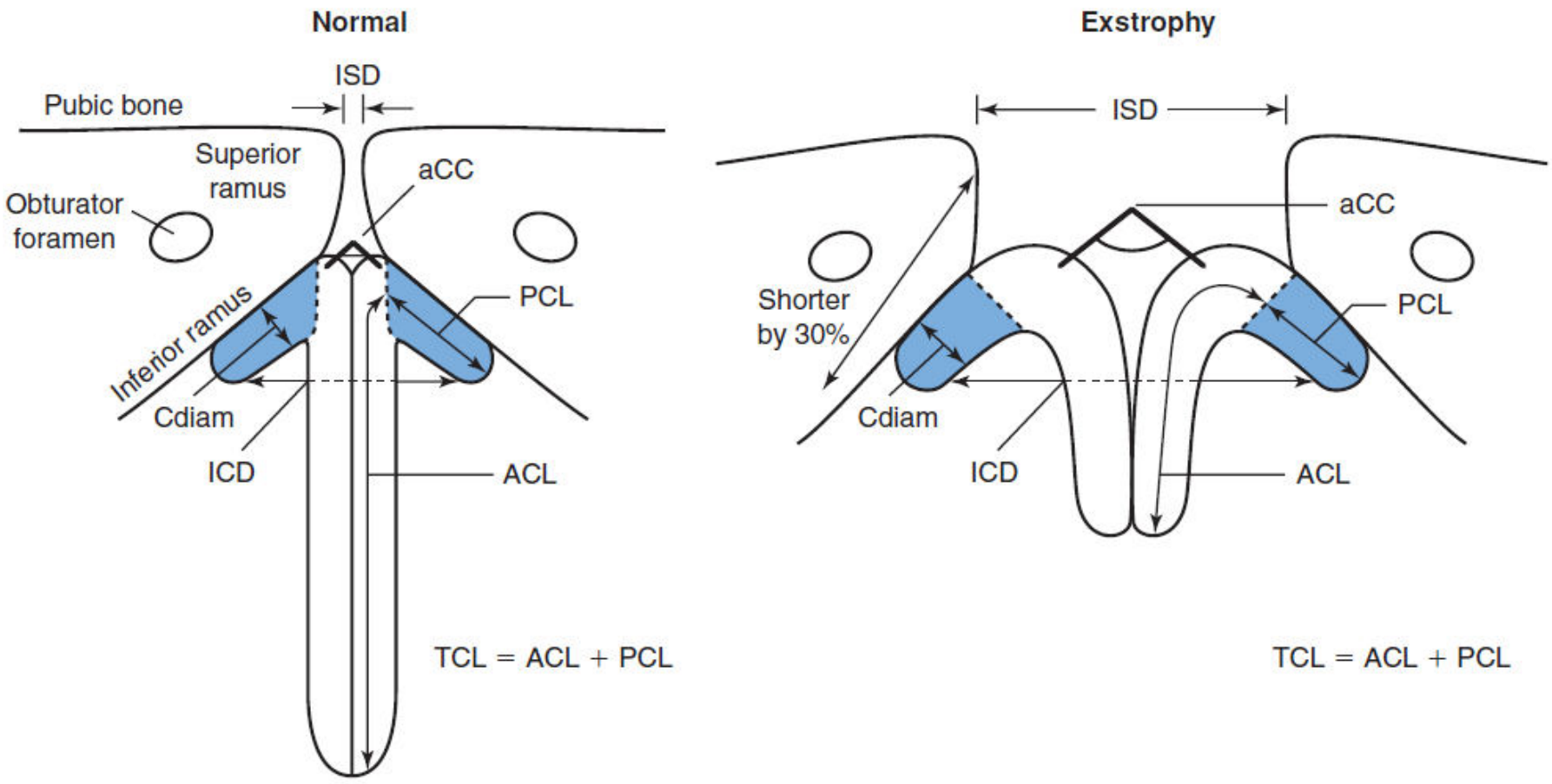
- Patients with cloacal exstrophy have associated anomalies more often than not.
- These anomalies can affect:
  - upper urinary tract
  - intestines
  - skeletal system
  - neurologic system.

Kidneys and upper urinary tract

- Renal anomalies can occur with bladder exstrophy
  - Cystic dysplasia
  - Ureteropelvic junction (UPJ) obstruction
  - pelvic kidney
  - Megaureter
  - renal hypoplasia
  - horseshoe kidney
- Vesicoureteral reflux (VUR) occurs almost universally.

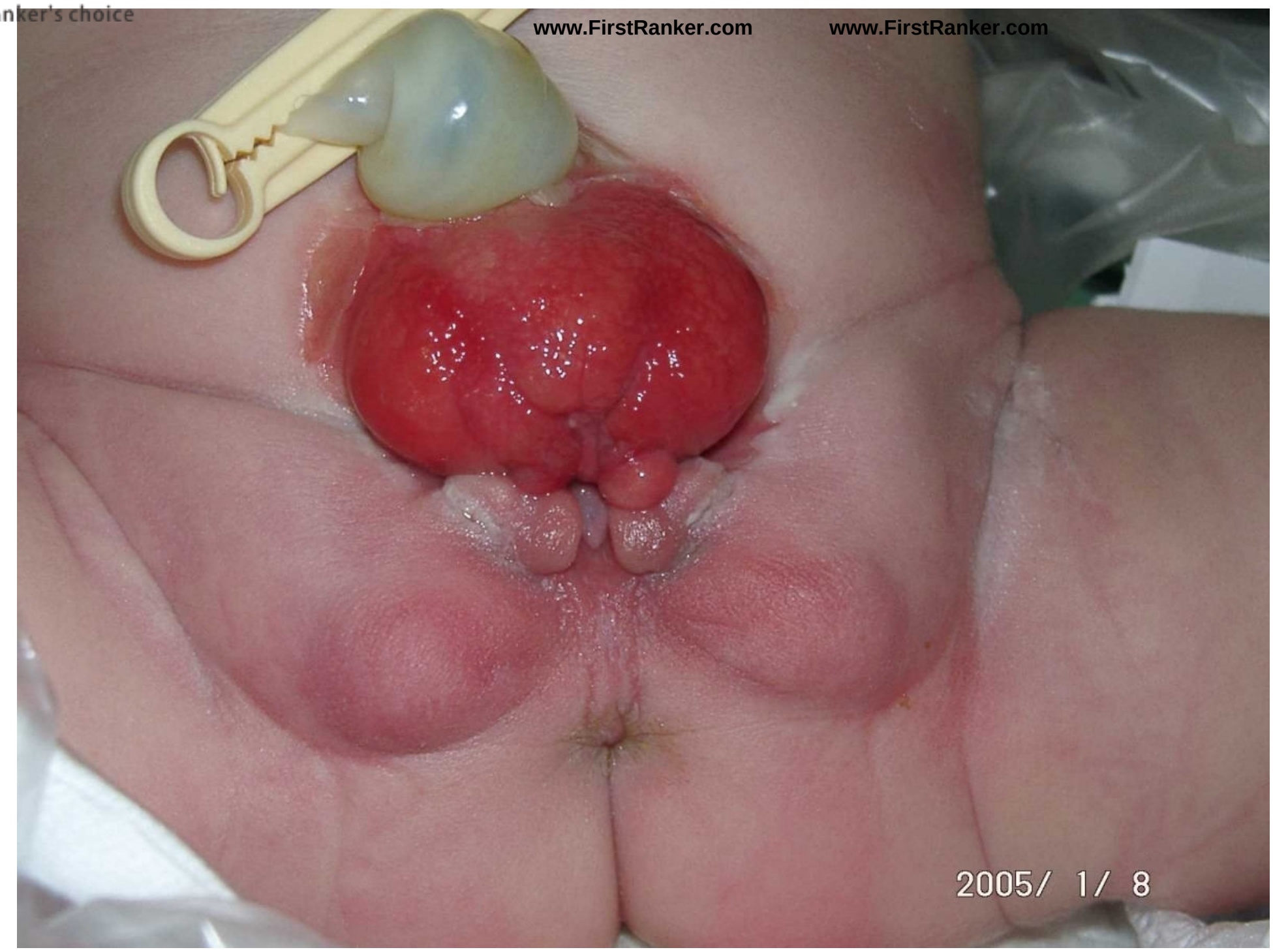
Genitalia

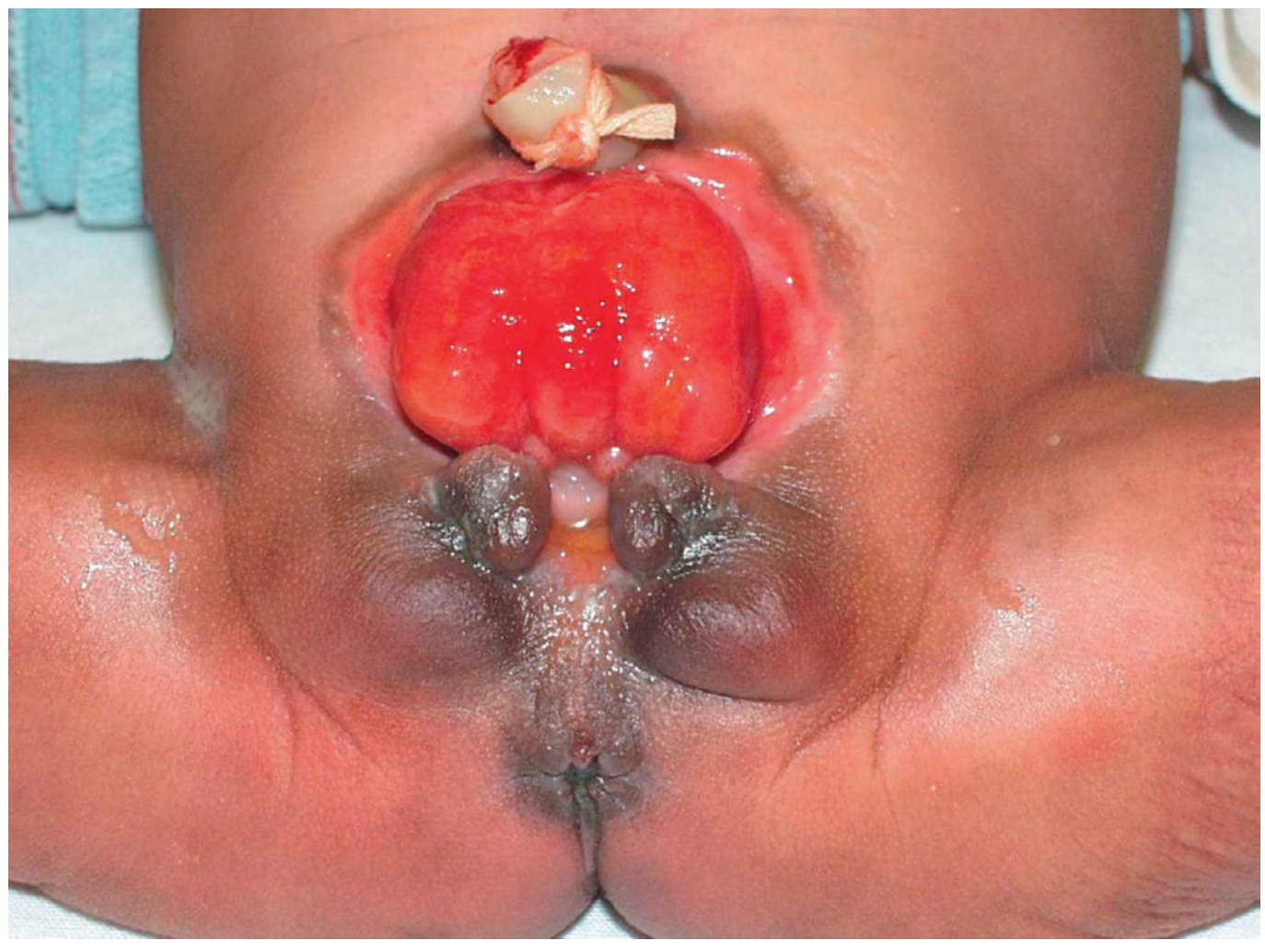
- In males:
  - the penis is broad and shortened because the corpora cavernosa are splayed laterally, attached to the separated pubic bones.
  - The penis is deflected dorsally and may have true intrinsic dorsal chordee
  - in most cases, the length of the penis and the size of the exstrophic bladder plate are inversely related



Penile and pelvic measurements in normal men and patients with exstrophy. ISD, intersymphyseal distance; aCC, corpora cavernosa subtended angle; Cdiam, corpus cavernosum diameter; PCL, posterior corporeal length; ICD, intercorporeal distance; ACL, anterior corporeal length; TCL, total corporeal length.

- The cavernosal nerves are located on the lateral aspects of the corporeal bodies.
- In the normal situation, these nerves can be found on the dorsal aspect of the penis after they traverse the posterolateral aspects of the prostate and the membranous urethra.
- The prostate is also incompletely formed in exstrophy.
- The scrotum is usually not affected
  - increased distance between the base of the penile shaft and the scrotum
  - broadening of the scrotum dependent on the degree of diastasis
- The testes may be undescended.
- Because of the underlying bladder neck anomalies, exstrophic males may have impaired fertility.
  - Retrograde ejactulation because bladder neck cannot close completely.
- In females:
  - Mons pubis is absent
  - Bifid clitoris
  - Anterior labia are laterally displaced although they fuse in the midline posteriorly.
  - The vagina and introitus are also displaced anteriorly from their usual position.
  - The vaginal opening may be stenotic.
  - Internal female genital structures (uterus, cervix, fallopian tubes, and ovaries) are unaffected in classic exstrophy.
  - Uterine prolapse as a result of deficient pelvic floor support can occur in the older exstrophy patient and poses particular problems with pregnancy.
    - Early primary bladder reconstruction with pelvic closure may decrease this risk.
    - Uterine suspension procedures such as sacro-colpopexy can be employed in these situations.



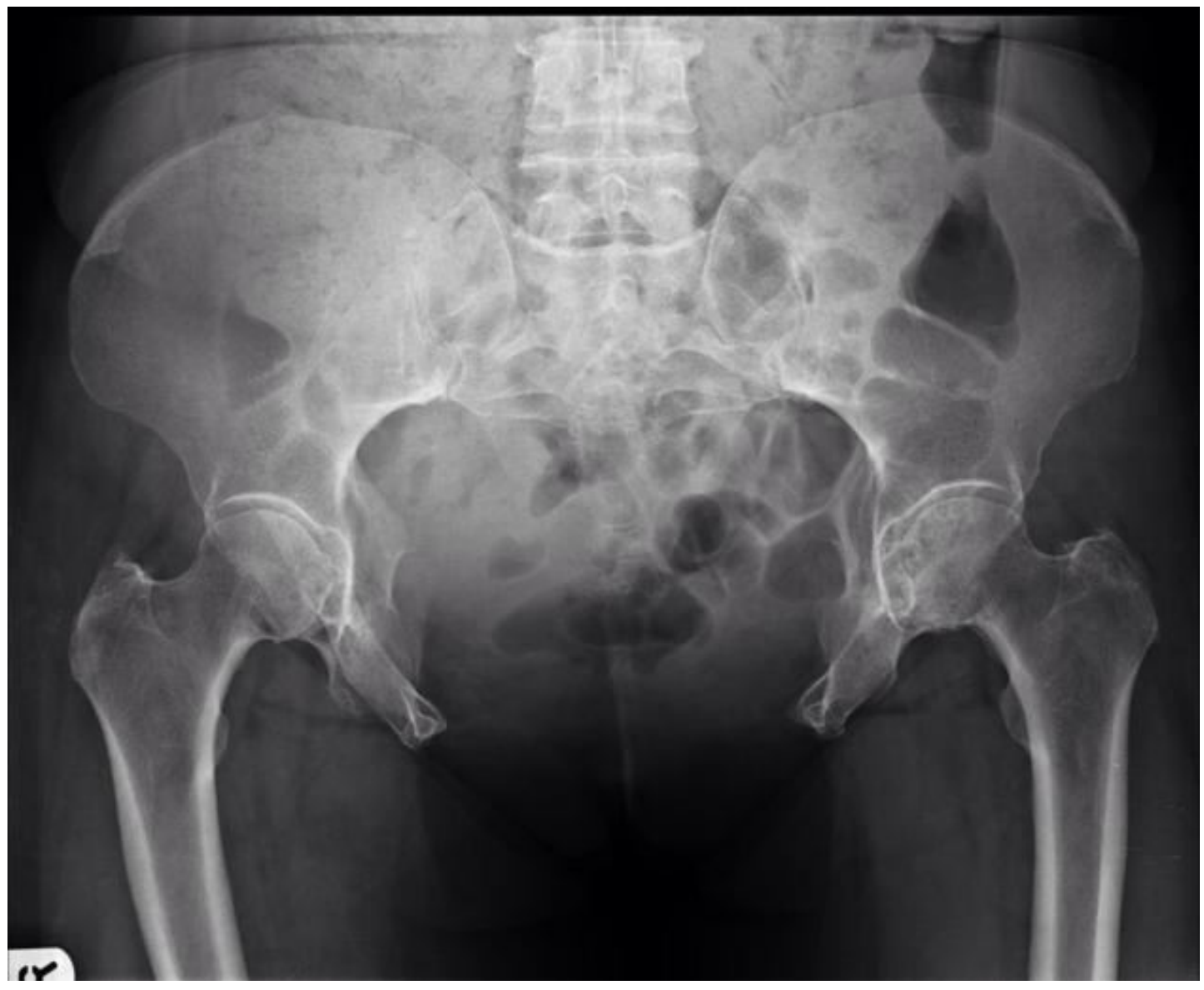


Anorectal and intestinal abnormalities

- The anus is often located anteriorly in the exstrophy complex.
- Few exstrophic patients will have insufficient anal continence due to the underlying abnormalities of the pelvic floor support structures including the levator ani and puborectalis muscles.
- In untreated patients rectal prolapse can also occur owing to insufficient pelvic floor support.

Skeletal abnormalities

- Diastasis of the pubic symphysis occurs as part of the exstrophy complex.
- This results from outward rotation of the innominate bones along both sacroiliac joints.
- Outward rotation of the pubic rami at the iliac and ischial junctions is also seen.



- Gait abnormalities in these children arise as a consequence of these bone abnormalities.

- Many of these children learn to ambulate with a wide waddling gait. This gait abnormality resolves as the children grow.

- Orthopedic procedures to re-approximate the pubis symphysis do not offer any long-term benefits to these patients from an orthopedic viewpoint.

- Osteotomies to re-approximate the pubis symphysis
  - increase the chance of successful primary bladder closure
  - have a significant role in securing continence
  - support of the pelvic diaphragm

Fascial abnormalities

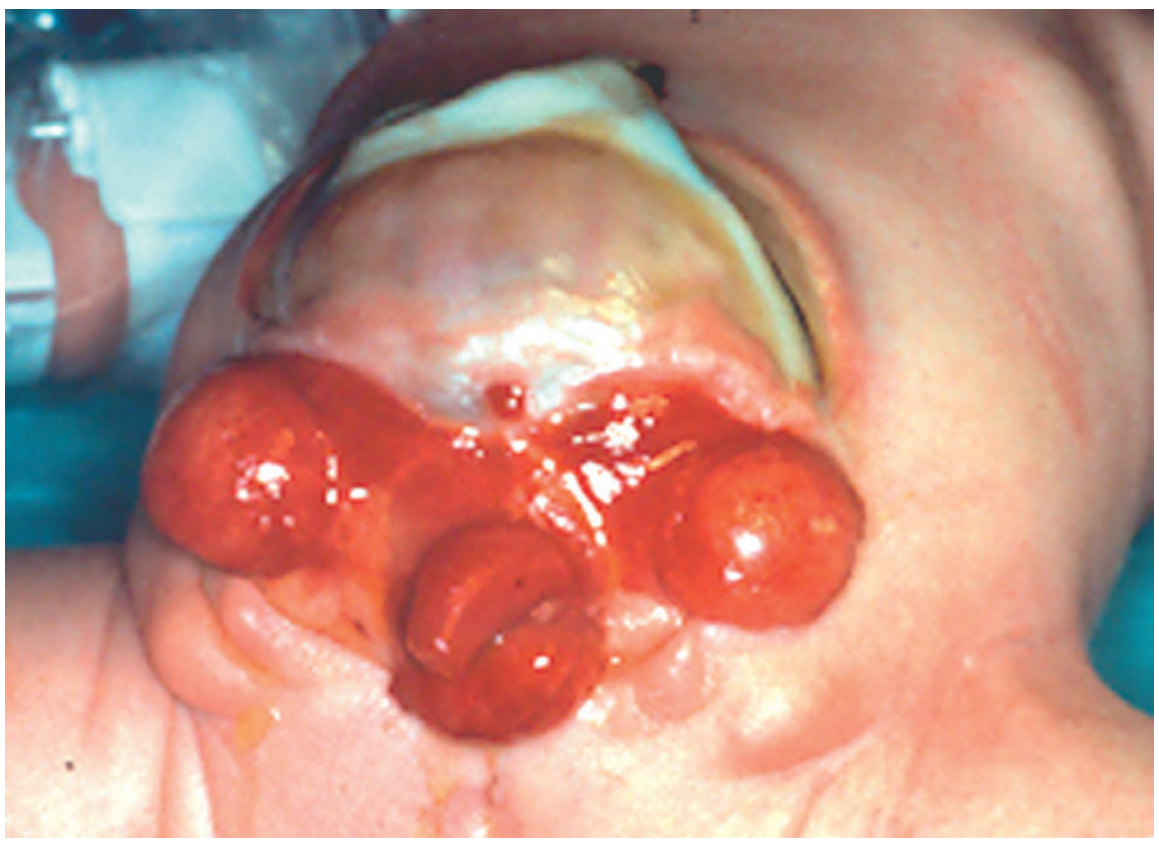
- Inguinal hernias are commonly associated with exstrophy in both male and female patients.
- Majority of these hernias occur indirectly.
  - occur as a consequence of the enlarged internal and external inguinal rings
  - lack of obliquity of the inguinal canal
- Rectus fascial defect
- Inferiorly, the pelvic floor support structures are also compromised.
  - At the inferior portion of the fascial defect, these patients possess an anteriorly located intersymphyseal ligament or band representing the attenuated urogenital diaphragm.

Neurologic system

- Spinal cord abnormalities
- Occult spina bifida and even myelomeningocele can be seen in combination with bladder exstrophy

Anatomic pathology: *Cloacal exstrophy*

- The bladder plate associated with cloacal exstrophy is divided in half by the hindgut plate.
- the hindgut plate represents the deformation in the development of the colon that occurs with cloacal exstrophy.
- Ileum enters and intussuscepts into the middle of the hindgut, creating the ‘trunk of an elephant’s face’ appearance with appendiceal appendages located laterally to give the impression of ‘tusks on the face of the elephant’.



Photograph and schematic drawing of a neonate with cloacal exstrophy. BP, bladder plate; C, cecal plate; CB, corporeal body; HG, hindgut; IL, ileum; O, omphalocele; UO, ureteral orifice

- With cloacal exstrophy, the bladder neck (internal urethral sphincter) and external urethral sphincter are not fully developed.

- However, because the innervation to these structures is usually intact, anatomic closure theoretically offers the possibility of achieving urinary continence.

- The urethral plate is characteristically short as well.

Associated anomalies

- **Kidneys and upper urinary tract**
  - Renal anomalies are much more common with cloacal exstrophy.
  - They include anomalies of location such as pelvic kidneys or crossed fused ectopia.
  - Horseshoe kidneys, renal agenesis, and UPJ obstruction may also occur.

- **Genitalia**
  - In cloacal exstrophy the penis is often separated into two hemiphalluses owing to the wide pubic diastasis.
  - Cryptorchidism is the rule with cloacal exstrophy.

  - For girls, in addition to the genital pathology described with bladder exstrophy, uterus didelphys and other fusion anomalies of the müllerian duct structures are seen in up to two-thirds of cloacal exstrophy patients.
  - Vaginal agenesis occurs in one-third of girls with cloacal exstrophy.

- **Anorectal and intestinal abnormalities**
  - Associated intestinal abnormalities specific to cloacal exstrophy include
    - imperforate anus
    - foreshortening of the midgut
    - bowel duplication
    - Malrotation
    - Intestinal atresia, and Meckel's diverticulum.
  - These are in addition to the exstrophy of hindgut, ileal intussusception, and exposed appendices that are considered part of the primary pathology of cloacal exstrophy.

- **Skeletal abnormalities**
  - Skeletal anomalies are seen in as many as 50% of patients with cloacal exstrophy.
  - Anomalies include congenital hip dislocation, talipes equinovarus, and a variety of limb deficiencies.

- **Fascial abnormalities**
  - The fascial anomalies associated with cloacal exstrophy include those described above for bladder exstrophy.
  - Further, omphaloceles often occur in association with cloacal exstrophy.

- **Neurologic abnormalities**
  - Neurologic involvement of the lower spinal cord in the cloacal exstrophy population is reported to occur in 50–100% of patients.
  - Most patients have lumbar or sacral cord involvement, but thoracic-level myelodysplasia has been reported.
  - Management of cloacal exstrophy in these situations must be coordinated with neurosurgical plans to close the neural tube defect.

Anatomic pathology: ***Epispadias***

- Epispadias can be considered the least severe form of exstrophy.
- It does not involve the body of the bladder.
- The urethra is represented as a plate of tissue located dorsally on the penis.
- The genital anomalies include lateral splaying of the penis and dorsal chordee in boys.
- In affected girls, the clitoris is bifid, the perineal body is broadened, and the vagina is anterior to its typical position.
- Widening of the pubic diastasis occurs as well.

- Importantly, the bladder neck is also frequently involved – it is often wide and incompetent. This directly affects the continence mechanism of these children and impacts the ability to achieve urinary continence.

- In boys with epispadias, primary continence is possible if the epispadias is located distally and the bladder neck is normally formed.

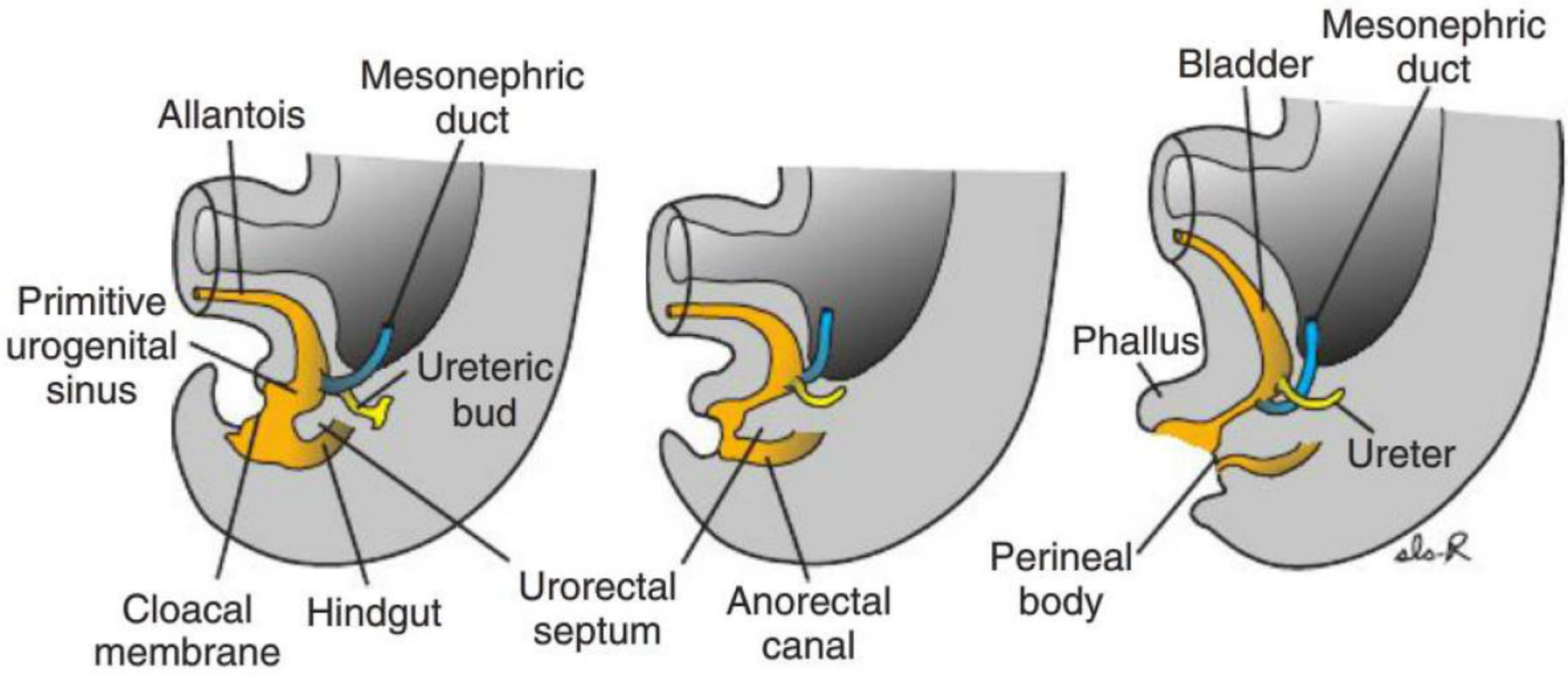
- In girls, however, continence is invariably affected to some degree because of the associated urethral and bladder neck ectasia.

EPIDEMIOLOGY

- The incidence of bladder exstrophy is estimated at between 1 in 10,000 and 1 in 50,000 live births.
- Higher male to-female ratio of between 2.3:1 and 4:1.
- Familial recurrence is approximately 1 in 100.
- Multiple reports of bladder exstrophy among identical twins have demonstrated variability in involvement of one or both twins.
- Subsequent siblings and the offspring of individuals with bladder exstrophy may be at increased risk of being affected.
- However, no clear pattern of inheritance has been characterized and no specific genetic or environmental factor that predisposes to bladder exstrophy has yet been identified.

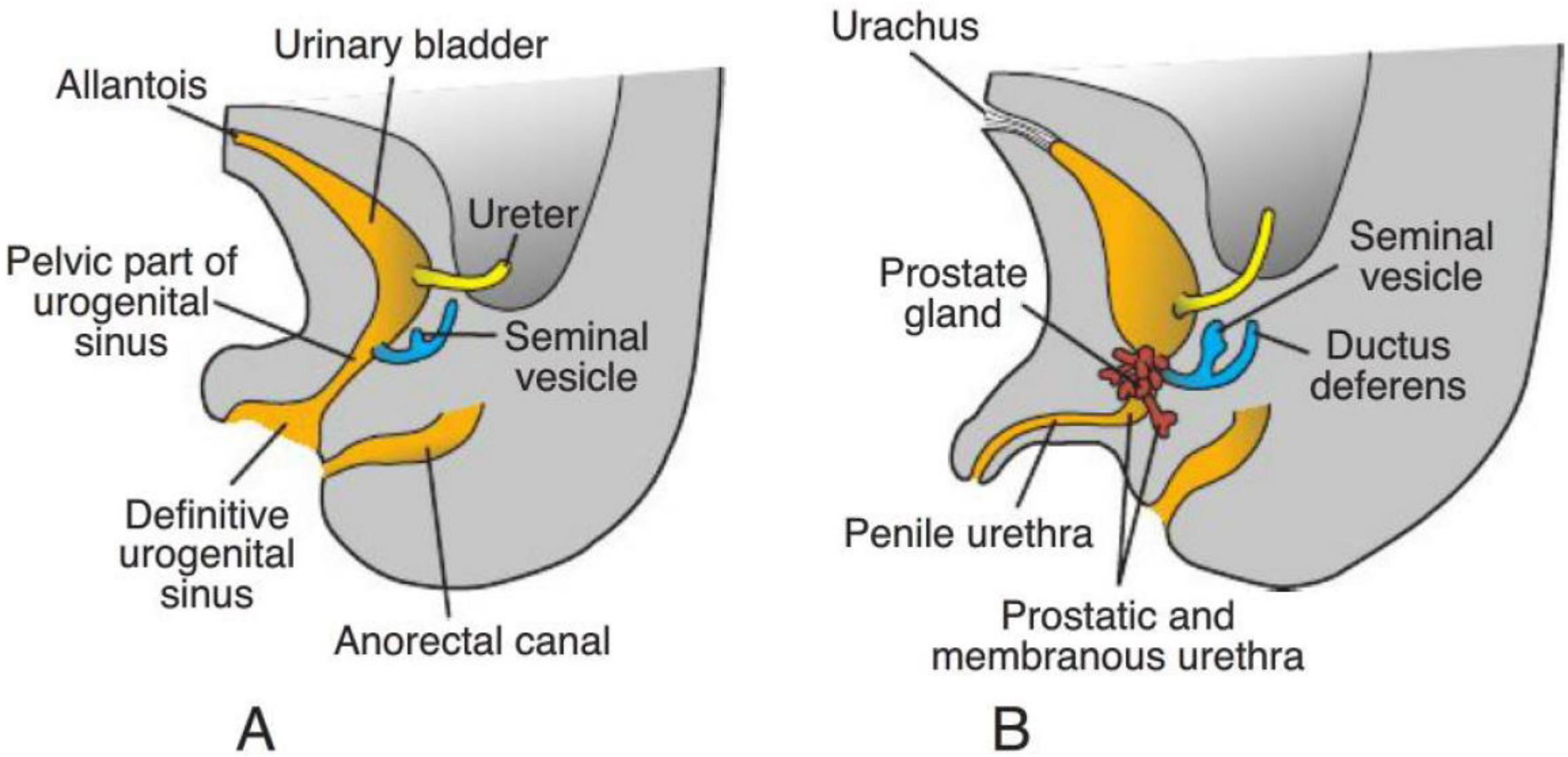
Embryology

- Abnormal development of the cloacal membrane, a bilaminar structure composed of endoderm and ectoderm that overlies the cloacal cavity at the caudal end of the germinal disk.
- In normal development, lateral ingrowth of mesoderm occurs between the two layers of the cloacal membrane during the fourth and fifth weeks of gestation.
- This results in formation of the lower abdominal wall and pelvis.
- Subsequent caudal growth of the urorectal septum results in its fusion with the cloacal membrane, thus fully separating the cloaca into the bladder anteriorly and the rectum posteriorly.



- The paired genital tubercles, which will give rise to the phallus, migrate medially to fuse in the midline.

- Normal perforation of the cloacal membrane occurs after fusion with the urorectal septum, at approximately the sixth week, resulting in formation of separate urogenital and anal openings.



- Migratory failure of the lateral mesodermal folds and abnormal overdevelopment of the cloacal membrane have both been proposed as potential causes of the prevention of normal mesodermal ingrowth to the cloacal membrane.

- The lack of adequate mesodermal reinforcement is thought to result in premature rupture of the cloacal membrane, the timing of which determines the extent of the abdominal wall defect and degree/severity of urogenital tract involvement.

- Rupture of the cloacal membrane after fusion with the urorectal septum results in bladder exstrophy, whereas rupture before fusion gives rise to the more severe presentation of cloacal exstrophy.

PRENATAL DIAGNOSIS

- The use of prenatal ultrasound (US) and MRI has improved the antenatal diagnosis of bladder exstrophy, allowing for appropriate parental counselling and planning of postnatal management.

- The prenatal diagnosis of bladder exstrophy may be suggested on US by failure to visualize the bladder in the presence of normal kidneys and amniotic fluid.

SURGICAL RECONSTRUCTION

- Surgical management of classic bladder exstrophy consists of
  - functional closure of the native bladder
  - closure of the epispadic urethra and genitalia
  - creation of a continence mechanism to allow for proper urine storage.

- Reconstruction may be accomplished in a multi- or single-stage (complete) repair
  - modern staged reconstruction of exstrophy (MSRE)
  - complete primary reconstruction of exstrophy (CPRE)

MODERN STAGED RECONSTRUCTION OF BLADDER EXSTROPHY

- A three-stage approach for the treatment of bladder exstrophy was first pioneered by Jeffs and Cendron in the 1970s.
- Stage 1 is performed at birth to protect the upper urinary tracts and assist later continent reconstruction.
  - It consists of early closure of the bladder, posterior urethra, and abdominal wall with or without osteotomy. The primary objective of functional closure is to convert the bladder exstrophy into a complete epispadias.
- Stage 2 is performed in later infancy and involves repair of the epispadias, with the goal of optimizing genital function and appearance, as well as increasing outlet resistance to promote bladder growth.
- Stage 3 is undertaken before school age and consists of bladder neck repair for continence and ureteral reimplantation for vesicoureteral reflux.

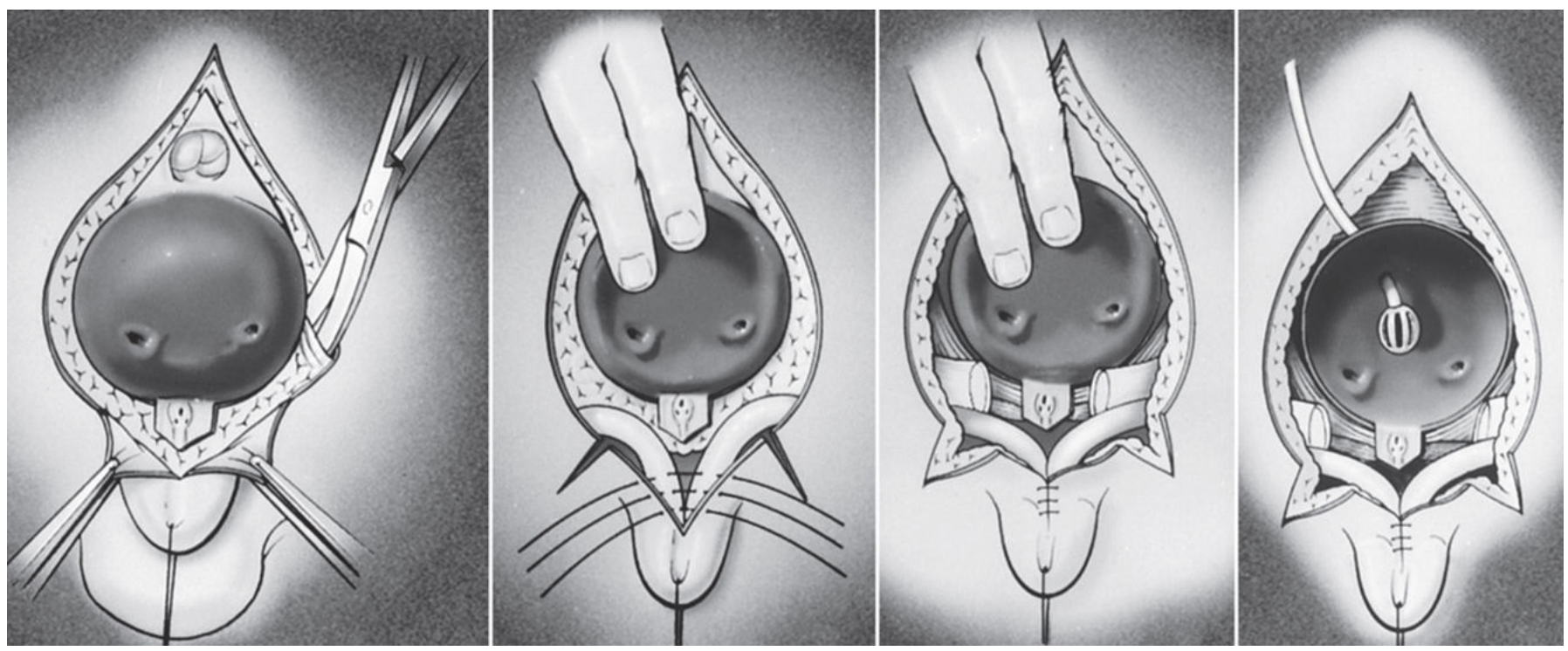
INITIAL MANAGEMENT

- At birth, the umbilical cord should be ligated with a silk suture to avoid irritation of the bladder surface from the traditional plastic clip.
- The exposed bladder mucosa should be moistened with saline and protected with a nonadherent sheet of plastic wrap (e.g., Saran Wrap).
- A complete physical examination is performed to rule out associated anomalies and to assess the size of the bladder plate and extent of the genital defect.
- Renal US may be obtained to exclude hydronephrosis and/or other upper tract abnormalities.
- Prophylactic antibiotics should be administered.

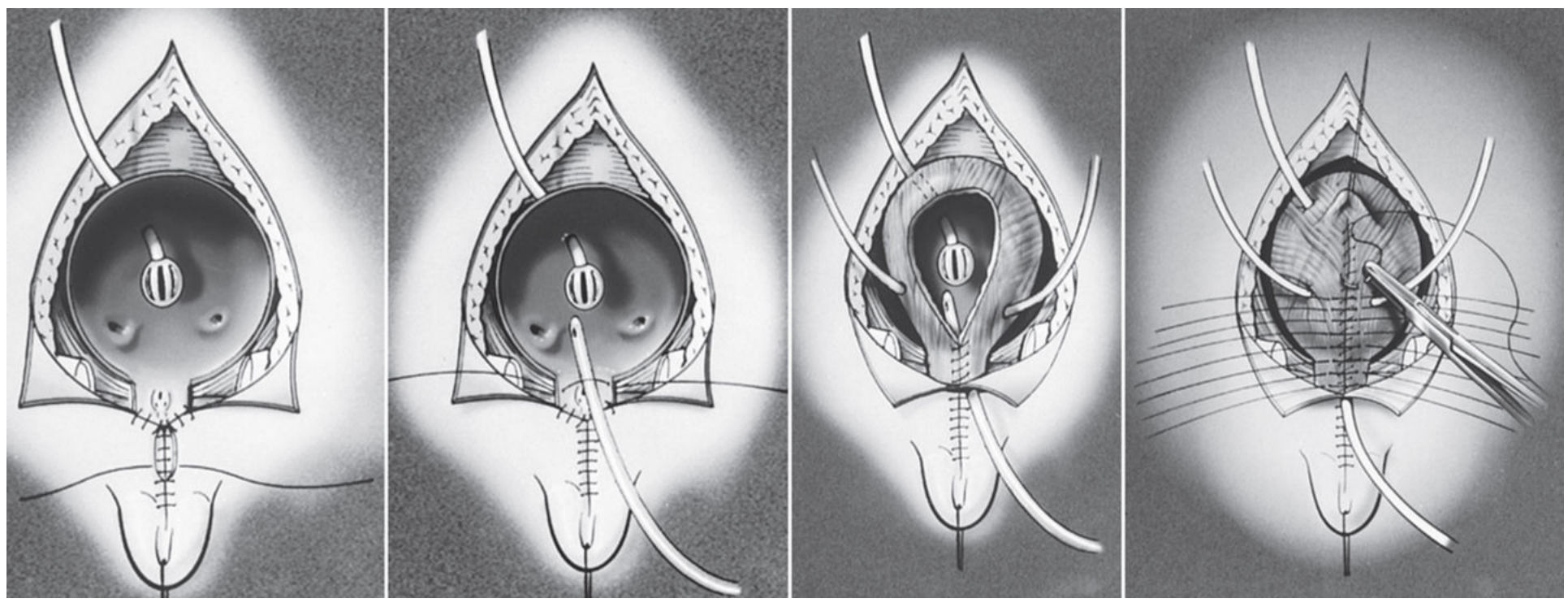
- Primary functional closure is generally undertaken in the neonatal period, which offers several potential advantages.
  - The pliability of the pelvic ring, in infants younger than 72 hours old, may obviate the need for osteotomy.
  - Early closure prevents further exposure and scarring of the bladder plate.

- Alternatively, delayed closure in combination with pelvic osteotomy may be performed.

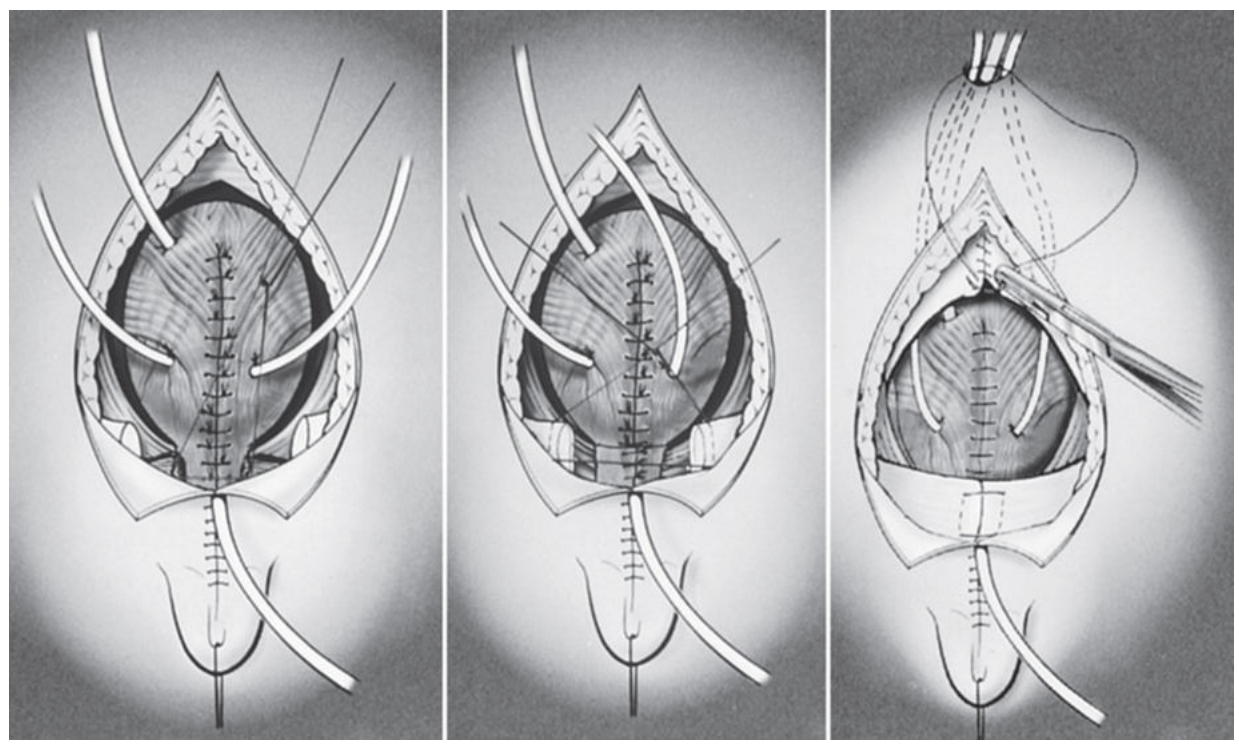
Stage 1



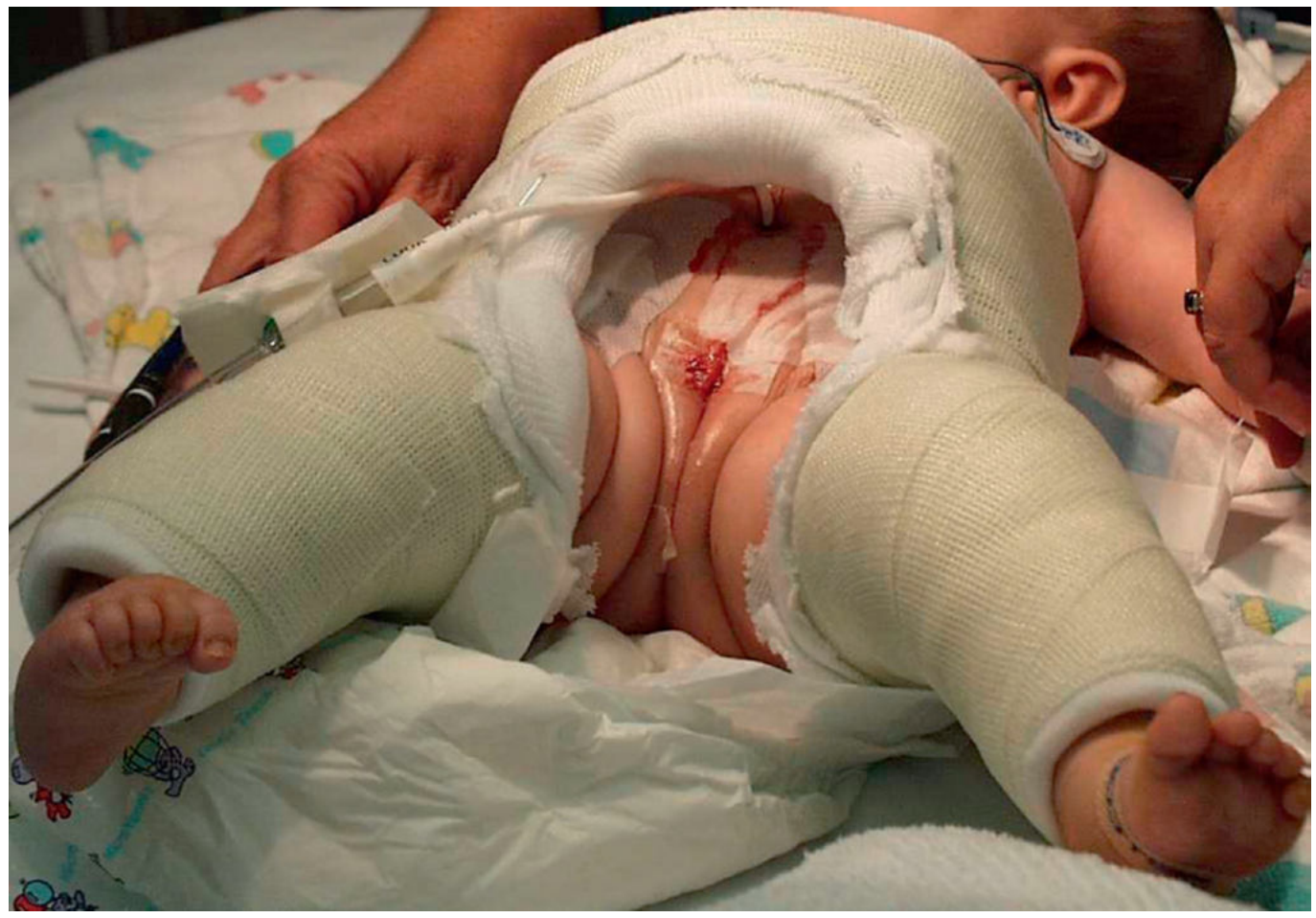
A, Completion of the dissection around the periphery of the bladder and the urethral plate.
B, Inversion of the bladder plate and approximation of the corpora as a first stage in epispadias repair. Also note the inferior paraexstrophy incisions.
C, Further closure of the skin over the corpora and their partial freeing from the pubis.
D, Placement of a suprapubic drainage tube



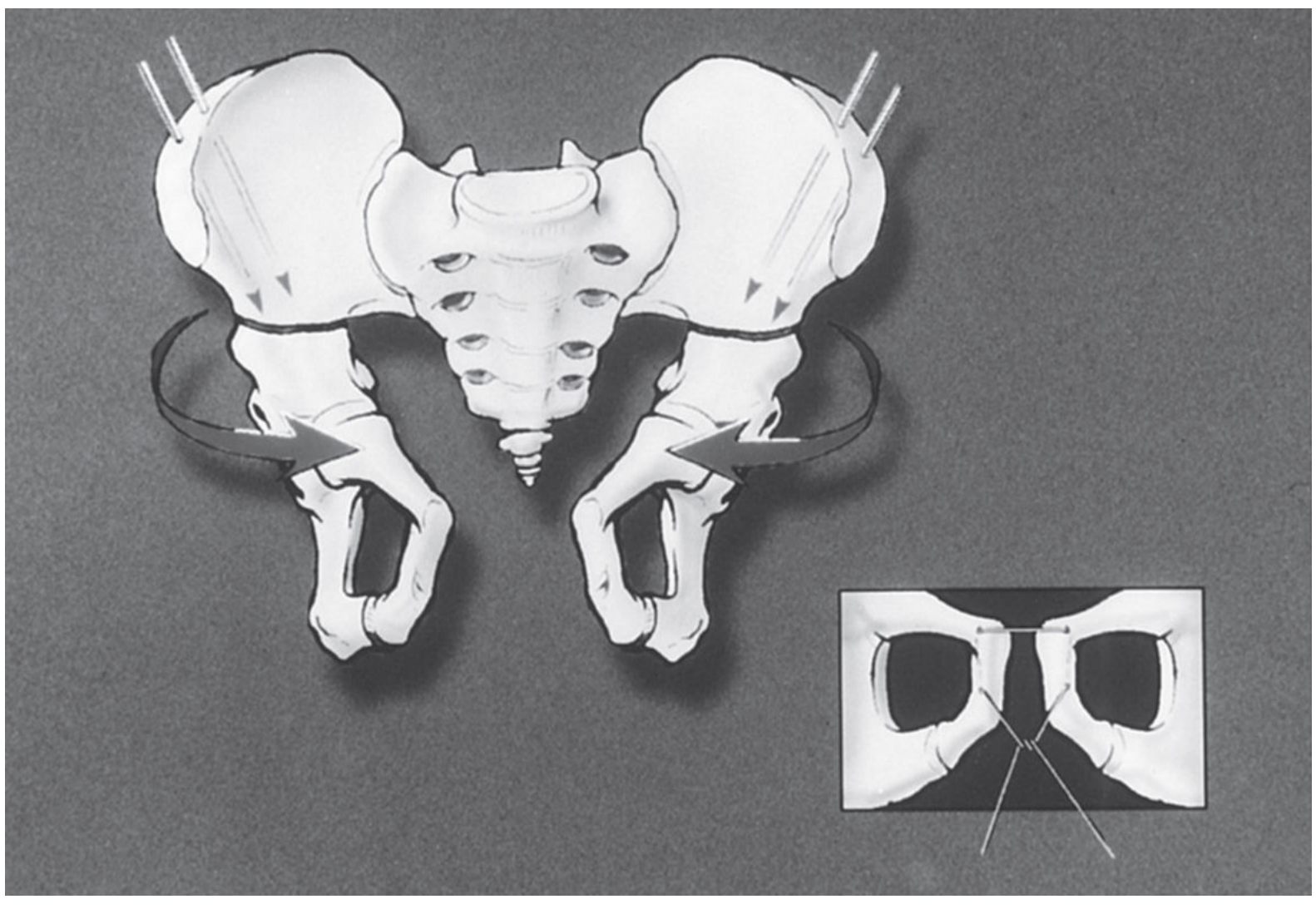
E, Further closure of the skin inferiorly, with approximation to the urethral plate. Creation of the para-exstrophy flaps is now evident.
F, The urethral plate is prepared for tubularization over a catheter.
G, The urethral plate is now tubularized, and ureteral catheters are placed bilaterally and brought out on each side of the bladder. The bladder is also in the process of being tubularized.
H, Completion of tubularization of the bladder and urethra, and location of the various drainage tubes.



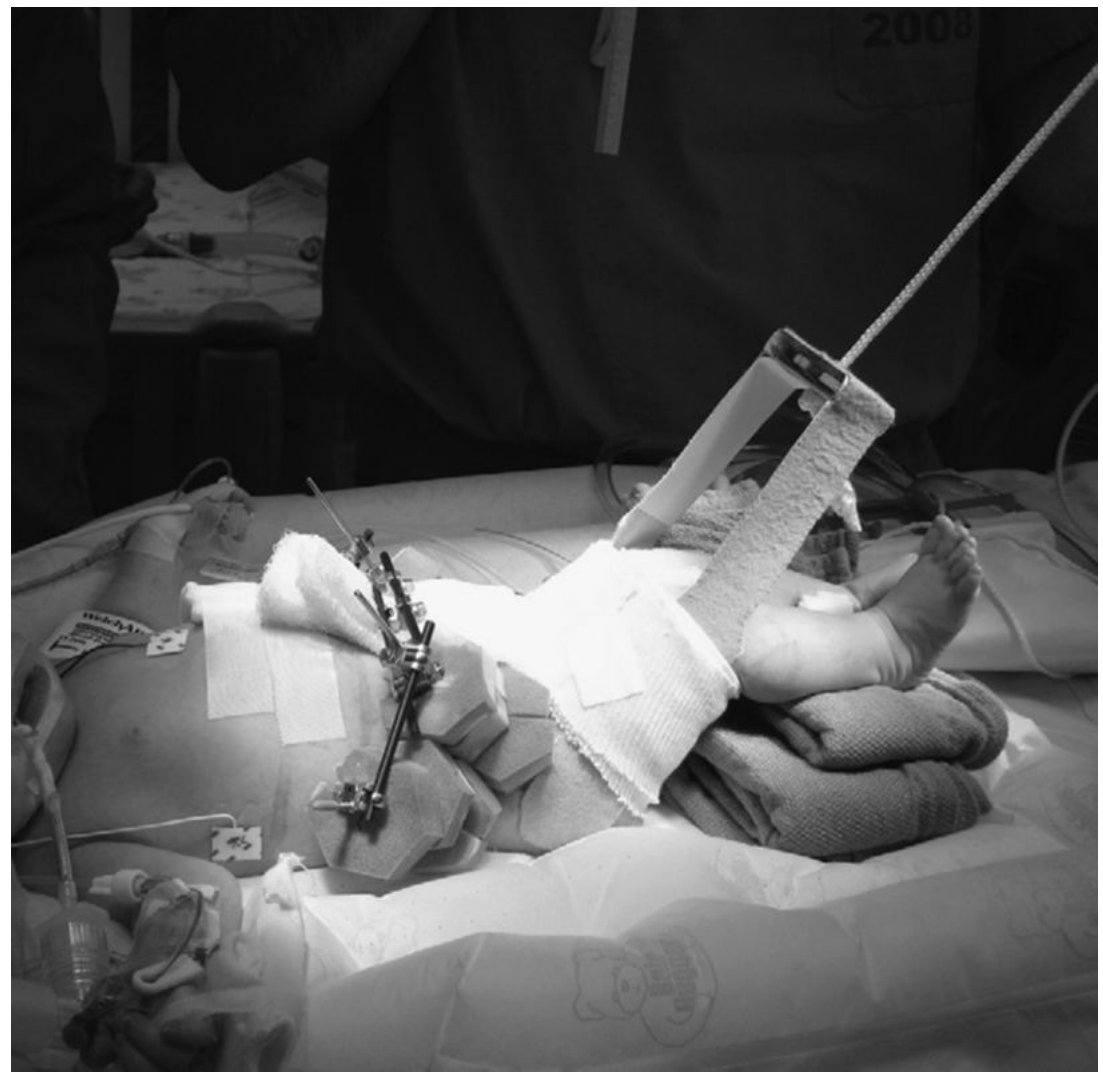
I, After two-layer closure of the bladder and urethral plate, the bladder is reduced into the pelvis and fixed with sutures.
J, Sutures are placed to encourage approximation of the pubic halves.
K, Drainage tubes are brought out superiorly, and fascia, subcutaneous tissue, and skin are approximated. Approximation of the pubis helps protect the bladder closure and the abdominal wall closure.



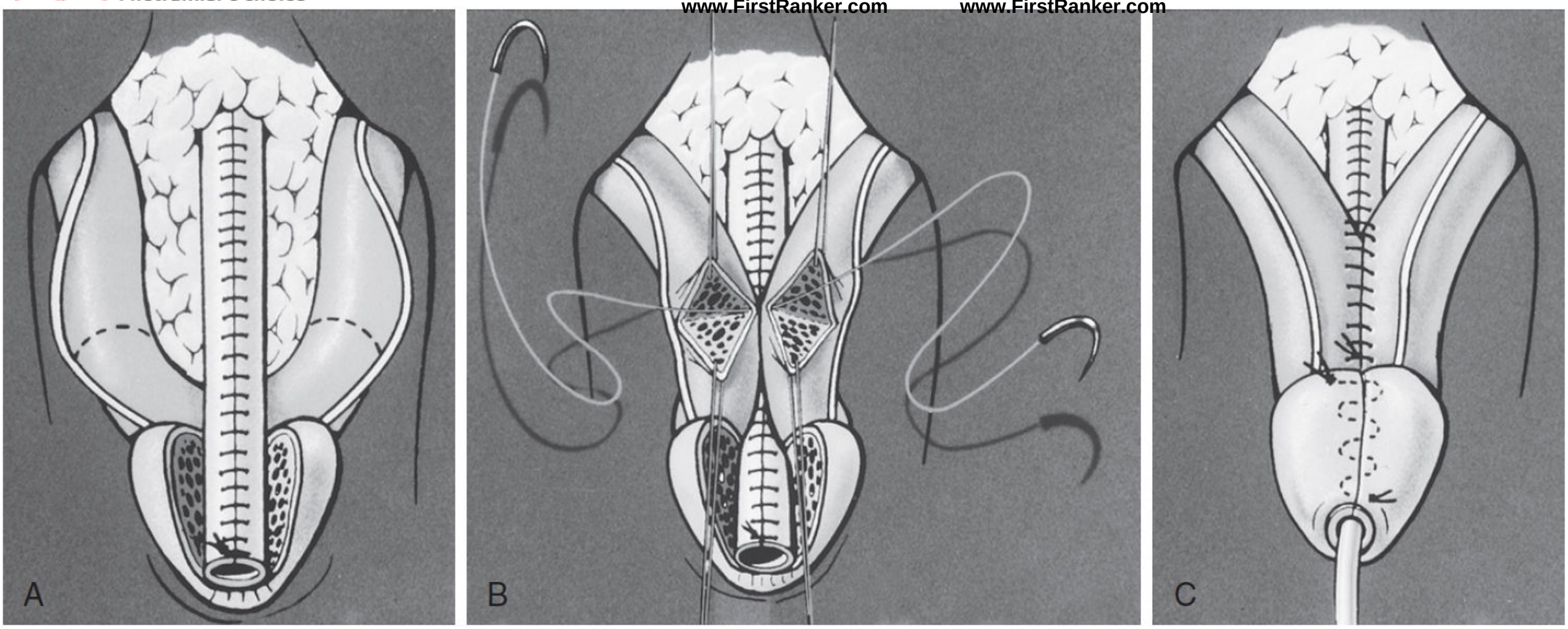
This photograph shows a spica cast that was applied to prevent external hip rotation and optimize pubic apposition in the early postoperative period.



External fixator pins are used to hold the pelvis, and the pubic halves are brought together in the midline.

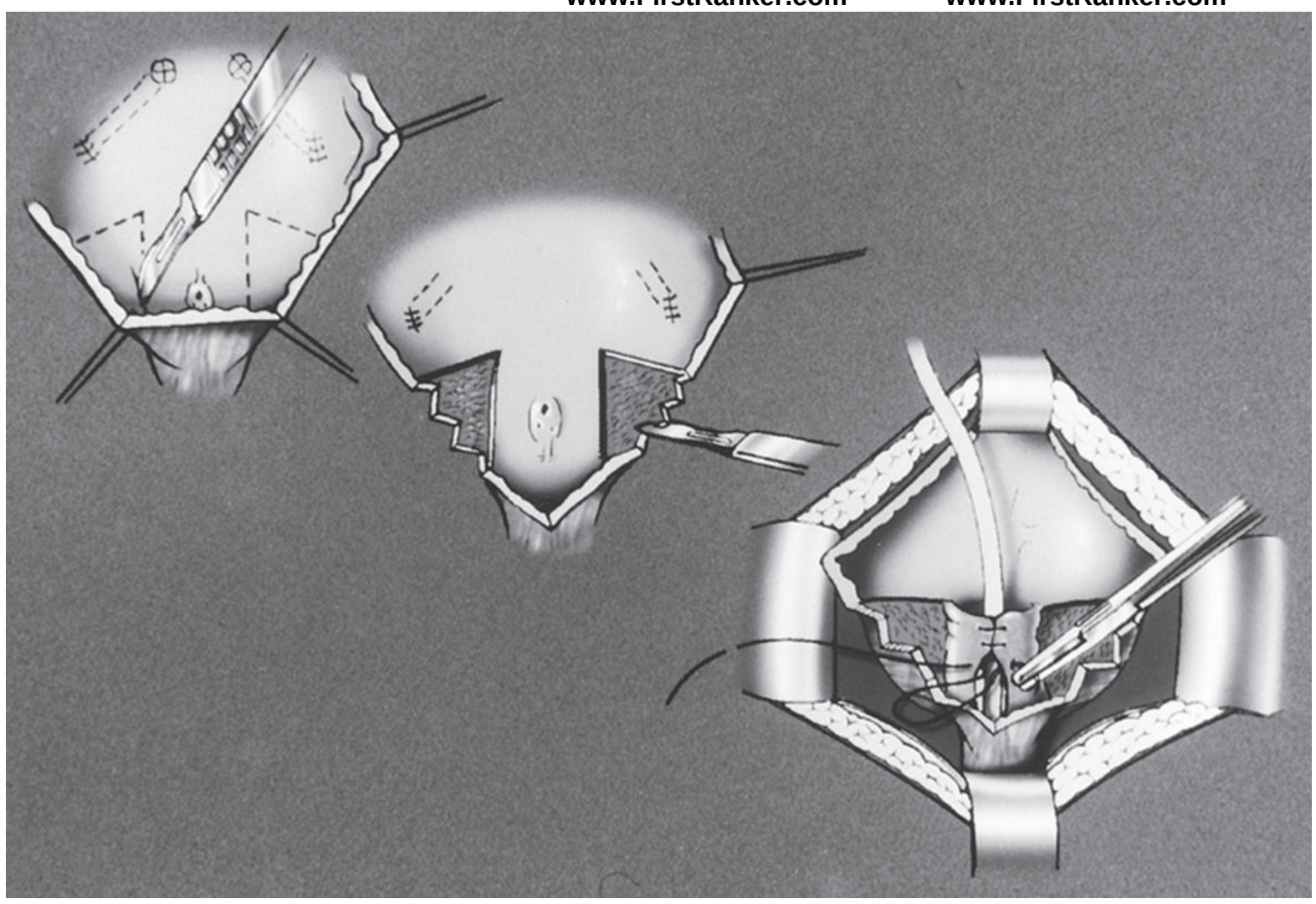


Stage 2



Cantwell-Ransley epispadias repair. A, The urethral plate is dissected from the corpora and is tubularized, taking care to
preserve the lateral blood supply of the urethra and the neurovascular bundles. B, Corporotomies are created at the midphallus, and the urethra is transposed to the ventral surface. C, The corpora cavernosa are rotated medially and reapproximated at the corporotomy sites, pulling the corporal bodies inward and providing coverage of the neourethra. This procedure permits further urethral lengthening, approximation of the corpora with preservation of the blood supply, and full coverage of the urethra.

Stage 3



Young-Dees- Leadbetter procedure for bladder exstrophy repair.
The ureters are appropriately reimplanted to avoid reflux. Triangular areas at the bladder base are then denuded, and the remaining muscle is tubularized over a catheter. This serves to lengthen the urethra and provides sufficient pressure to encourage the development of improved bladder capacity without causing urethral obstruction.

SINGLE-STAGE RECONSTRUCTION: COMPLETE PRIMARY REPAIR OF EXSTROPHY

- Mitchell and Grady minimized the number of required operations by combining bladder closure with epispadias repair at birth in a technique known as complete primary repair.

- Major potential benefits of this approach include
  - earlier creation of bladder outlet resistance, theoretically leading to normal cycling and improved bladder capacity and functionality as the patient grows.

- Major principles of CPRE include total penile disassembly and division of the intersymphyseal band, which enables posterior positioning of the bladder, bladder neck, and urethra.

URINARY DIVERSION

- Urinary diversion, in the form of a bowel conduit or reservoir, may ultimately be required for patients with insufficient bladder plate or after reconstructive efforts have been unsuccessful.

OUTCOMES AND COMPLICATIONS

- The most devastating complication of bladder closure is dehiscence.
  - Major contributing factors include wound infection, abdominal distension, bladder prolapse, and loss of ureteral and/or suprapubic catheters within 6 days of closure.
  - Urinary diversion, reclosure of the bladder as a urethral tube for later augmentation, or delayed repair of the bladder may be performed.
  - If not performed in the initial setting, pelvic osteotomy is frequently necessary for successful reclosure.

- Urinary incontinence remains a significant problem for up to 30% of bladder exstrophy patients.
  - In the case of bladder neck incompetence, injectable bulking agents, bladder neck sling or artificial urinary sphincter have all been applied.
  - Bladder neck reconstruction or formal closure of the bladder neck, with the creation of a catheterizable channel, can also be performed.

- In cases where incontinence is secondary to insufficient bladder capacity, augmentation cystoplasty remains the most viable treatment option.

- Following epispadias repair, the most common complication is urethrocutaneous fistula, which ranges from 2% to 26% in modern series.

- The incidence of adenocarcinoma of the bladder in adults with bladder exstrophy has been estimated to be 250 times that of the normal population and is likely due to chronic inflammation, infection, and metaplasia of an exposed bladder.

- The development of adenocarcinoma and transitional cell carcinoma of the bladder is also a potential risk in those patients who have undergone augmentation cystoplasty.

- Fertility in patients with bladder exstrophy and epispadias was studied by Shapiro and colleagues, who surveyed 2500 patients.
  - Among these, 38 men had successfully fathered children and 131 women had given birth.
  - Diminished fertility rates among males may be secondary to retrograde ejaculation, though libido and erectile function appear to be normal.
  - Female patients face a significant risk of uterine prolapse.

SURGICAL RECONSTRUCTION IN CLOACAL EXSTROPHY

- The surgical management of cloacal exstrophy is typically undertaken in the newborn period (48 to 72 hours).
- The main goals of reconstruction include
  - secure abdominal wall and bladder closure
  - preservation of renal function
  - prevention of short gut syndrome
  - creation of functionally and cosmetically acceptable genitalia
  - attainment of urinary and fecal continence.

- All approaches begin with initial separation of the intervening cecal plate from the two bladder halves, closure of the omphalocele, and hindgut preservation.
- Currently, after tubularization of the exstrophied cecum, it is recommended that the hindgut segment be brought out as an end-colostomy.
- The hemi-bladders are dissected and then reapproximated in the midline.
- Further management based on individualised approach.

Conclusion

- For the past 20 years, survival among patients with cloacal exstrophy has exceeded 90%.
- Death is typically related to complications related to extreme prematurity, renal agenesis, or other complex malformations that are incompatible with life.
- Compared with those with classic exstrophy, however, cloacal exstrophy patients face additional challenges of achieving bowel and bladder continence secondary to the need for anal reconstruction and the associated defect of spinal dysraphism.
- It must be stressed that multiple operations are the rule, and these patients will likely face significant medical, psychologic, and social challenges throughout their lives.
- Advancements in medical and surgical management continue to improve functional and quality of life outcomes in these patients, but it is important that these individuals remain under the care of a multidisciplinary team of providers who can offer medical care, psychologic support, and lifelong follow-up.