Structural Anomalies of the Bladder and External Genitalia

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12.1 Introduction

Genitourinary tract anomalies are some of the most common forms of congenital anomalies. A thorough appreciation of embryology as well as sexual differentiation is imperative to understanding these disease processes and their related assessment and management techniques. The scope of these anomalies and the manner in which they present is vast; therefore, we have attempted to present these disease processes in a concise yet comprehensive manner. The underlying common theme is the goal of the practitioner to provide refunctionalization of the urinary tract and/or genitalia in these patients.

12.2 Bladder Anomalies

Genitourinary anomalies are commonly diagnosed in the perinatal period, but congenital bladder anomalies are relatively rare. Usually these anomalies are caused by outlet obstruction or are part of a more serious syndrome. When detected prenatally, these anomalies are usually separated into dilated or nondilated anomalies.

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12.2.1 Dilated Bladder Anomalies

The presence of a large or dilated bladder usually suggests either a functional or mechanical outlet obstruction. Examples of obstructive causes of dilation include posterior urethral valves, urethral atresia, or other causes of extrinsic obstruction. Nonobstructive causes of a dilated bladder might be neurologic disorders in which the patient is unable to empty the bladder and congenital megacystis in which vesicoureteral reflux and continuous cycling of urine between the upper and lower tracts causes bladder dilation [1].

12.2.2 Nondilated Bladder Anomalies

Cloacal and bladder exstrophy result in the nonvisualization of the bladder in a fetus due to incomplete closure of the bladder template [2]. This can be distinguished from bladder hypoplasia by the presence of normal levels of amniotic fluid. Bladder hypoplasia can be due to a number of causes including bypass of urine due to ureteral ectopia, abnormalities of kidney development with decreased urine production, or decreased bladder outlet resistance such as in severe epispadias. Complete bladder agenesis is extremely rare; there have been only 60 reported cases in English literature [3]. This is incompatible with life unless the ureters are drained ectopically [4].

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12.2.3 Other Bladder Anomalies

Other bladder anomalies that are detected postnatally are usually compatible with life and only detected incidentally. Congenital bladder diverticula are herniations of the bladder mucosa between defects in the smooth muscle fibers [5]. They may be caused by bladder outlet obstruction or congenital defects. Most diverticula are asymptomatic, so the true incidence is difficult to determine [6]. However, patients with symptomatic diverticula and associated genitourinary dysfunction such as vesicoureteral reflux should undergo surgical intervention.

Bladder and urethral duplication can occur as complete or incomplete and may be associated with duplications of the external genitalia and gastrointestinal tract [7].

12.2.4 Urachal Anomalies

The urachus serves as a form of bladder drainage through the umbilical cord that obliterates prior to birth in normal development. The urachus is a tubular structure that extends from the dome of the bladder to the anterior abdominal wall and is flanked by the umbilical arteries on either side. When this structure fails to obliterate, one of four anomalies occurs based on the extent of failed obliteration to include the following: patent urachus, umbilical-urachal sinus, urachal cyst, or vesicourachal diverticulum [8]. Males tend to outnumber females, from 1.2:1 to 2:1 [9, 10].

A completely patent urachus presents with drainage from the umbilicus, delayed cord stump healing, or an erythematous cord stump [11]. Ultrasound can support this diagnosis by identifying a fluid-filled structure from the dome of the bladder to the level of the cord stump. A patent urachus may also present with infection or abscess – the most common organisms being *Staphylococcus aureus, Escherichia coli, Enterococcus, Citrobacter,* and *Proteus* [9]. A patent urachus should be treated with surgical excision with the addition of antibiotic coverage if it is associated with infection.

An umbilical-urachal sinus occurs when the urachus obliterates at the level of the bladder but remains patent at the umbilicus resulting in a continuously draining sinus. This must be differentiated from a fully patent urachus, usually done with ultrasonography. The treatment is surgical excision [8].

A urachal cyst is comprised of a portion of urachus that remains tubularized without connection to either the bladder or the umbilicus. This cyst can intermittently drain into the bladder or the umbilicus and may present as an umbilical abscess or a UTI. If left unrecognized, an infected urachal cyst can perforate into the peritoneal cavity, causing peritonitis [12]. Again, ultrasonography is used for diagnosis, but may require other imaging such as CT or MRI in older patients to better evaluate the extent of the disease. Traditional treatment entails initial surgical drainage and antibiotics with subsequent surgical excision of the entire urachal remnant [13].

A vesicourachal diverticulum occurs when the urachus obliterates almost completely with the exception of a portion near the bladder dome. Typically, these lesions are asymptomatic as they tend to have a wide neck that prevents stone formation or infection from occurring within the diverticulum. They are usually diagnosed incidentally on radiographic imaging for other purposes. There is no need for intervention for this particular finding unless the patient is symptomatic, such as with development of infection or stones within a small-necked diverticulum [14].

12.3 Neuropathic Bladder

12.3.1 Myelomeningocele

Myelomeningocele is the most common of all myelodysplasias or spinal dysraphisms in children and is the most common cause of neuropathic bladder dysfunction in children [14]. Development of the spinal canal begins on the 18th day of gestation and closes in a caudad to cephalad fashion, complete by day 35. Mesoderm in-growth over the developing spinal cord is necessary for closure of the canal; otherwise, an

open lesion is noted, most often in the lumbosacral area with decreasing incidence in the thoracic and cervical regions [15].

Neural injury and associated lower urinary tract dysfunction are related to an exposed spinal cord and tension on the spinal cord as the spinal cord comes to its final location in the canal during fetal development [16]. The conus medullaris is almost always involved due to the high relative incidence of lumbar and lumbosacral defects [15]; therefore, nerve roots originating from this area that would normally innervate the bladder are almost always involved and cause varying degrees of dysfunction. Other related features that may affect urologic management include the following: hydrocephalus, paralysis/mobility, and spinal deformities [15].

Hydrocephalus is a typical finding in these patients, with severity directly correlated to the extent of spinal cord involvement. More pronounced intellectual disabilities tend to go hand-in-hand with more pronounced physical disabilities. Patients with severe disabilities often lack the physical capabilities and cognitive skills necessary to perform clean intermittent catheterization (CIC) or deploy an artificial urinary sphincter, thereby precluding these common interventions and introducing challenges for caregivers. Spinal deformity such as kyphoscoliosis and mobility limitations must also be taken into consideration for planning of long-term management strategies. Fortunately, the trend toward early closure of the spinal defect has recently been demonstrated to decrease the incidence of hydrocephalus and may improve neurologic function in patients with myelomeningoceles [16].

12.3.1.1 Assessment

The bony spinal lesion is not predictive of the extent of the spinal cord lesion and resultant neurologic and lower extremity dysfunction [17], so thorough neonatal assessment is imperative. Renal ultrasonography and measurement of postvoid residual urine are assessed as early as possible. If the patient demonstrates inability to empty satisfactorily or has evidence of upper tract deterioration such as loss of kidney parenchyma, CIC should be initiated [18]. A serum creatinine, urinalysis, and culture should also be obtained [15].

Urodynamic studies (UDS) and voiding cystourethrogram (VCUG) are delayed until the spinal defect has been closed, and it is prudent to transport the patient and position him or her appropriately for the study [19]. These studies provide vast amounts of information including radiologic appearance of the upper and lower urinary tracts, identification of patients at risk for renal impairment due to bladder dysfunction, or outflow obstruction. They also provide anatomic and functional baselines to which future studies can be compared. As high as 15–20 % of patients have abnormal GU tract radiologic findings, usually due to spinal shock or bladder outlet obstruction [14]. UDS provide information about bladder and urethral sphincter function that may categorize patients as having either high or low risk for upper tract deterioration.

12.3.1.2 Management

As previously mentioned, CIC is an essential component of GU tract management in a significant number of patients with neuropathic bladders. Indications include detrusor muscle-external urethral sphincter dyssynergia, elevated bladder pressures, and/or grade III or higher vesicoureteral reflux [14]. This intervention has been shown to prevent upper tract deterioration, provides continence in a majority of patients, and reduces the need for bladder augmentation [20].

In patients with vesicoureteral reflux (VUR) secondary to high bladder pressures from neuropathic dysfunction, CIC lowers intravesical voiding pressures. When coupled with anticholinergic pharmacotherapy, this can serve to lower detrusor filling pressures and increases bladder compliance which may result in resolution of reflux [20].

The goal of therapy is to maintain bladder stability as well as stable renal function via adequate bladder capacity, a compliant detrusor muscle, periodic emptying at a low pressure, and continence. When this cannot be achieved by CIC and anticholinergic medications, a variety of surgical procedures are available to meet specific needs as follows:

- Failure to perform CIC due to body habitus, mobility issues, discomfort, or anatomic concerns – surgical creation of a catheterizable channel or vesicostomy on the lower abdomen.
- Detrusor noncompliance or impaired/high-pressure bladder capacity – bladder augmentation (reserved for refractory cases in older patients).
- Conduit urinary diversions are no longer the first-line surgical in managing these patients and are reserved for severely debilitated patients or those who have failed other modalities.

12.3.2 Spina Bifida Occulta

Occult spinal dysraphism, or spina bifida occulta, is a group of congenital defects of spinal column formation that do not result in an open defect. These make up about 10 % of all congenital spinal dysraphisms and include tethered cord, lipomeningocele, diastematomyelia, and intraspinal cysts [21]. A majority of these patients have a normal neurologic exam in the neonatal period, but may later develop signs of neurologic impairment such as gait abnormalities, decreased perineal sensation, voiding dysfunction, or back pain during periods of rapid growth. An underlying spinal cord defect is often signaled by a cutaneous lesion such as a dimple, tuft of hair, or abnormal gluteal cleft in 90 % of these patients [22].

Forty to ninety percent of spina bifida occulta patients have some variety of voiding dysfunction on urodynamic testing [14, 23]. The defect may be of upper or lower motor neuron origin or a combination of the two. Early detection with MRI and early intervention allow reversal or at least stabilization of the lesion.

12.3.3 Sacral Agenesis

Sacral agenesis is defined as the absence of two or more vertebral bodies and is often associated with a variety of anorectal anomalies. Evaluation of the bony spine, and spinal cord if indicated, should therefore be performed in any patient with anorectal malformations or if clinical suspicion exists, e.g., patients with buttock wasting, especially in infants of diabetic mothers or mothers with gestational diabetes. The extent of vertebral deformity is not predictive of the spinal cord lesion or associated voiding dysfunction, and a reported 25 % of these children have no signs of neurologic dysfunction on urodynamic testing [24]. However, 35 and 40 % show an upper or lower motor neuron deficit, respectively [24]. In these patients, upper tract imaging and cystography are indicated, especially in the setting of a history of urinary tract infections. Management depends on the neurologic deficit with goals of protecting renal function and achieving appropriate quality of life endpoints such as continence.

12.4 Exstrophy-Epispadias Complex

The exstrophy-epispadias complex is a spectrum of abnormalities thought to arise from maldevelopment of the lower abdominal wall during the early part of gestation that includes the following:

- Bladder exstrophy – open bladder plate (always associated with a bifid clitoris in females and an epispadic urethra in both sexes)
- Cloacal exstrophy – both the bladder and bowel are open plates on the low abdominal wall
- Primary penile epispadias – partial or complete open plate of the urethra on the dorsal surface of the penis, comprised of three subtypes based on location of the opening of the urethra without associated exstrophy:
  - Glandular epispadias – opening is located distally on the glans penis.
  - Penile epispadias – opening is located at any location on the shaft of the penis.
  - Pubic or penopubic epispadias – opening is located at the junction of the base of the penis and the abdominal wall.

These are relatively rare defects, with incidence of each as follows: 1 in 10,000 to 1 in 50,000 for bladder exstrophy; 1 in 120,000 for primary epispadias; and 1 in 300,000 for cloacal exstrophy [25, 26]. It occurs predominantly in

males, with a reported male to female ratio from 2:1 to 6:1 [25, 27]. This condition represents a challenge to pediatric urologists given its low incidence and complex surgery needed to correct bladder and genital deformities.

There are many hypotheses regarding the etiology and embryologic defects that occurs to cause exstrophy. Current theories include failure of migration of mesoderm to the cloacal membrane [28], persistence of the cloacal membrane [29], and failure of the lateral body wall folds to meet in the midline [30]. There appears to be a familial component as the risk of bladder exstrophy in the offspring of a parent with exstrophy is about 1 in 100 [31]. Other theories regarding the etiology of exstrophy such as genetic defects and perinatal exposure are currently being explored [32, 33].

Prenatal diagnosis is possible as early as 18 weeks' gestation with fetal ultrasound. Sonographic features include inability to visualize urine in the fetal bladder, a bulging bladder plate or an apparent lower abdominal mass, a foreshortened penis, widening of the pubic ramus, and a low-set umbilicus [2]. These defects can easily be confused with other abdominal wall defects such as omphalocele or gastroschisis, but the use of 3D ultrasonography and MRI has improved diagnostic accuracy. The importance of prenatal diagnosis is for parental counseling and possible preparation for delivery at a specialized exstrophy center to allow for timely surgical intervention.

12.4.1 Bladder Exstrophy

Classic bladder exstrophy is exposure of the bladder plate and urethra beneath a low-set umbilicus. Associated maldeveloped structures include split rectus abdominis muscles, an open pelvic ring or pubic diastasis, and a foreshortened penis or bifid clitoris as the corporal bodies must traverse the pubic diastasis to meet in the midline (Fig. 12.1a, b). In males, testes are usually in a normal scrotal position, but the anus may be located

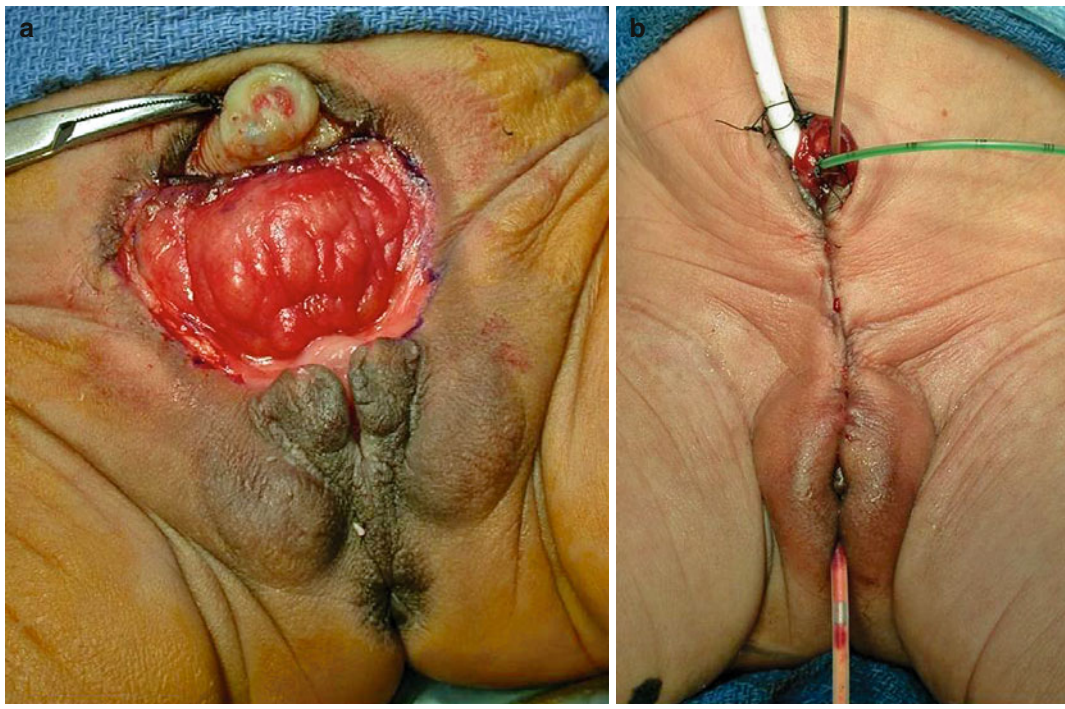

Fig. 12.1 (**a**) Bladder exstrophy and epispadias in a female. Note the exposed bladder plate and bifid clitoris. (**b**) The same patient after exstrophy closure

more anteriorly due to failure of development of both the lower abdominal wall and pelvic ring.

There are typically few associated anomalies with the exception of inguinal hernia, which occurs in up to 80 % of boys and 15 % of girls [34]. These babies are usually born full term without many significant medical comorbidities, so emergent surgical intervention is usually not warranted. However, timing of bladder closure is controversial, with some advocating immediate closure and others advocating delayed closure based on findings that later closure does not negatively affect overall bladder growth rates [35].

12.4.2 Cloacal Exstrophy

Unlike classic bladder exstrophy and epispadias, children born with cloacal exstrophy are often born prematurely and may be affected by the following associated anomalies: sacral agenesis or spinal dysraphism with related neurologic findings, cyanotic heart disease, renal agenesis or ectopia, orthopedic deformities of the lower extremities and pelvis, and small bowel defects such as malrotation or duodenal atresia [35]. Children born with cloacal exstrophy should have thorough evaluation to identify these possible comorbidities. Repair of life-threatening deformities such as cardiovascular or bowel defects may necessitate delay of exstrophy repair. In this case, the bladder and/or bowel plates are protected from desiccation or injury by cling wrap, and the umbilical stump is tied off to avoid trauma from clamps.

Severe genital deformities in males with cloacal exstrophy have historically presented a difficult challenge to both parents and pediatric urologists. If the genitalia could not be reconstructed to a functional and cosmetically acceptable male form, patients were assigned to female gender. In this case, they would also undergo simultaneous bilateral orchidectomy with vaginoplasty at a later date. Newer surgical techniques allow for better approximation of the corporal bodies in penile reconstruction, reducing the need for gender reassignment [36].

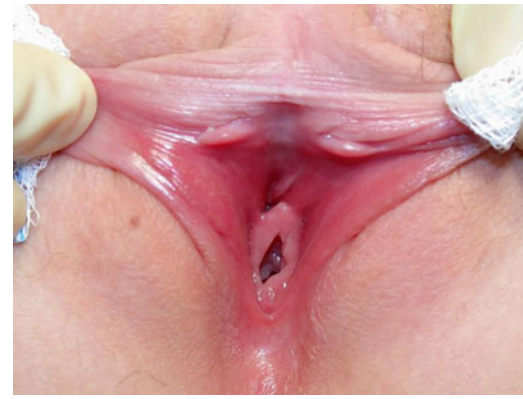

Fig. 12.2 Female epispadias. Note the bifid clitoris

12.4.3 Epispadias

Primary epispadias is rarely detected prenatally, but is usually detected at birth in males. Seventy percent of male epispadic patients have complete epispadias and associated incontinence due to incompetent sphincter mechanisms [37]. However, the meatus may be located at any point along the penile shaft; the more distal the meatus, the less likely the patient to have associated bladder neck and sphincter defects with incontinence. Associated anomalies include dorsal chordee in males, pubic diastasis, inguinal hernia, and vesicoureteral reflux.

Females may have delayed diagnosis as this is a rare entity and may be missed during routine examinations. These patients usually present later in life with stress incontinence or failure to complete toilet training (Fig. 12.2). Surgical repair is aimed at restoring normal voiding and continence as well as providing acceptable cosmesis.

12.4.4 Treatment and Outcomes

Though bladder exstrophy-epispadias is not a lethal anomaly, it has many obvious hygiene and social implications for pursuing repair. On the other hand, some cases of untreated cloacal exstrophy can result in death due to dehydration, malnutrition, and electrolyte abnormalities [38]. The goals of reconstruction are closure of the abdominal wall defect with or without closure of

the pelvic ring, urinary continence, preservation of the upper tracts, functional and aesthetically acceptable genitalia, and low-pressure urine storage. Staged reconstruction is usually required to obtain these outcomes in more severe cases [39].

Rates of urinary continence vary by both defect and use of differing definitions of the term. Most authors reporting continence rates do not specify whether this means complete continence, continence with catheterization and/or meds, or applies to daytime versus nighttime continence [40].

Sexual function and libido is usually preserved in cases of bladder exstrophy and epispadias, though fertility in males with exstrophy can be significantly reduced due to disruption of the ejaculatory ducts during lower tract reconstruction or retrograde ejaculation. Female fertility is preserved but may require surgical augmentation of the introitus to allow vaginal intercourse [41]. Fertility and sexual function in cloacal exstrophy repair is dependent on whether gender reassignment has occurred and whether phallic reconstruction in boys is successful. Girls tend to have normal fertility rates; delivery by Caesarian section is recommended [41].

Kidney damage can be detected in up to 25 % of patients as a result of reflux, recurrent infections, and vesicoureteral reflux [42]. However, the rate of renal insufficiency is estimated to be only about 10 % [37].

12.5 Hypospadias

Hypospadias is an association of features that results from abnormal development of the ventral portion of the penis. This typically presents with an abnormal ventral opening of the urethral meatus with or without hypoplasia of the corpus spongiosum and urethra, ventral chordee or curvature of the penis, and an incomplete, hooded prepuce. This incomplete penile development is thought to occur as a result of altered androgen influence via decreased production by the fetal testis, decreased androgen sensitivity in the developing tissues, or early cessation of androgen stimulation prior to completion of genital development [43].

12.5.1 Incidence and Etiology

Hypospadias is a relatively common anomaly with a reported incidence of 0.3–0.8 %, though there is some variation in data reported from different countries [44]. The incidence appears to be increasing in the USA, England, Hungary, and Norwegian countries [45]. Proposed theories for the increasing incidence are related to the known effects of androgens on development of hypospadias. Environmental contamination with estrogens from insecticides, pharmaceuticals, and plant estrogens might explain the rising incidence and increasing numbers of more severe forms of hypospadias [46]. The familial rate of hypospadias is about 4–10 %, which suggests that hereditary factors may be responsible for the defect [47].

There is an association between undescended testicles and hypospadias, with an overall incidence of approximately 7 % [48]. In a large number of these patients, there is an underlying genetic or phenotypic sexual abnormality, so disorders of sexual development should be investigated. This is especially true in cases of severe proximal hypospadias and/or bilateral cryptorchidism [49].

12.5.2 Classification

Standard classification of hypospadias is based on anatomic location of the urethral meatus. As hypospadias is the result of arrested development of the ventral portion of the penis, the meatus can be located anywhere along this surface, from the perineum to the glans (Fig. 12.3). This may also be associated with absence of the frenulum, incomplete fusion of the urethral plate and corpus spongiosum, as well as lack of development of the ventral portion of foreskin. Planning surgical intervention should take into account both the location of the urethral meatus as well as need for reconstruction or correction of these associated abnormal features.

12.5.3 Assessment

Patients tend to present with ventral chordee (curvature) of the penis, hooded foreskin, and

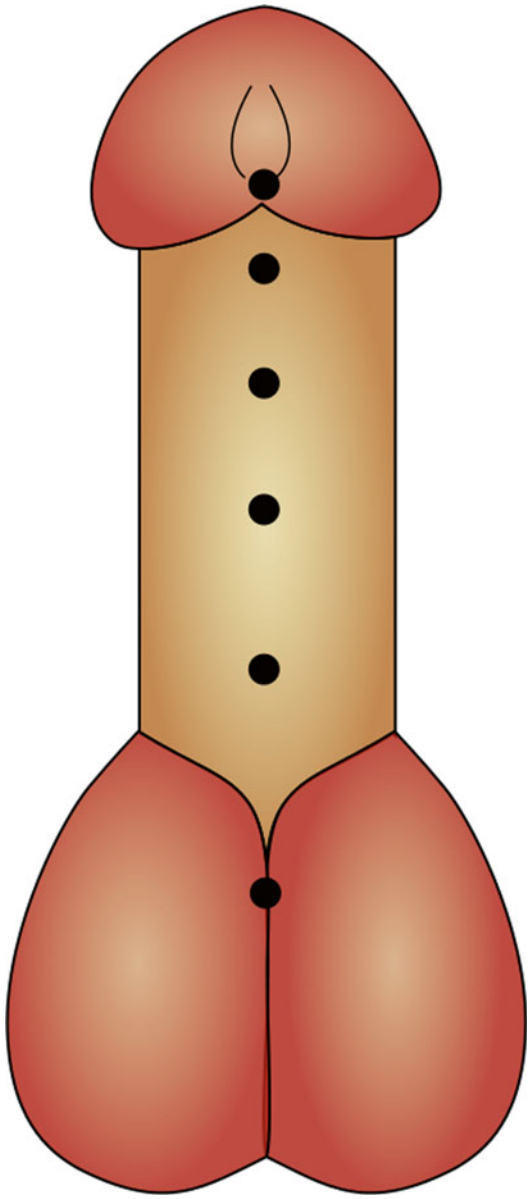

Fig. 12.3 Classification of hypospadias from most distal to proximal: glanular, coronal, distal, mid shaft, proximal, and perineal (Illustration courtesy of David A. Hamilton, Jr., M.D)

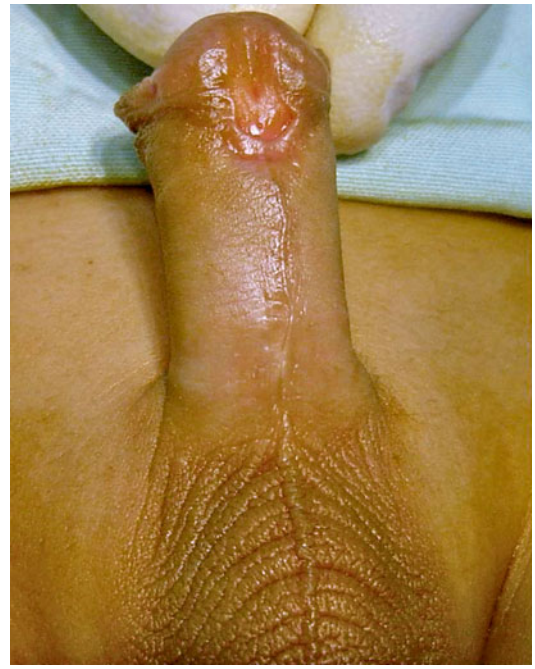

Fig. 12.4 Distal, or coronal, hypospadias

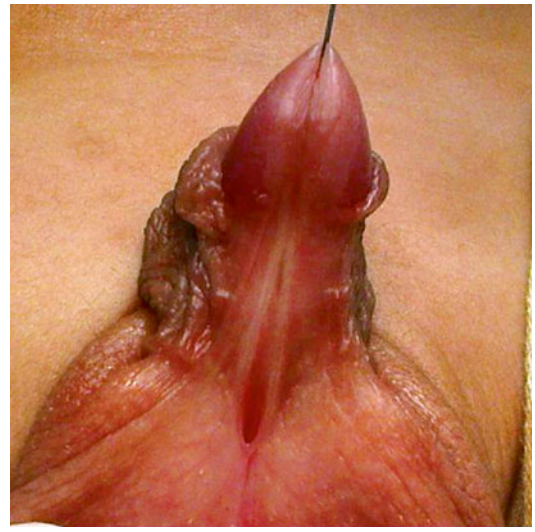

Fig. 12.5 Proximal, or penoscrotal, hypospadias

a stenotic ventral meatus. However, it is not uncommon for a patient to have incidental diagnosis of hypospadias at the time of circumcision when development of the prepuce has not been altered. The urethral meatus may be located in a variety of positions as previously mentioned, but 70–80 % of boys with hypospadias have a meatus located on the glans or distal shaft of the penis (Fig. 12.4), 20–30 % will have a mid-shaft location, and the remainder will have more severe defects with proximal location such as scrotal or perineal [50] (Fig. 12.5). If a patient presents with severe proximal hypospadias or hypospadias and cryptorchidism, a karyotype

should be obtained and evaluation for disorders of sexual development (DSD) should be undertaken as there is an association between endocrine dysfunction in hypospadias and DSD [50].

12.5.4 Management

The optimal timing of surgical intervention is controversial. The American Academy of Pediatrics Section on Urology recommends that the repair be complete by age 6–12 months as this allows correction of the defect before awareness of it causes long-term emotional or psychosexual impairment [51].

There are a variety of methods for hypospadias repair, and the techniques have been evolving over the last several decades. Despite numerous options for approaching the repair, the goals of repair are urethroplasty, correction of chordee or ventral curvature, and management of the foreskin either by circumcision or reconstruction.

12.6 Abnormalities of the Testis and Scrotum

12.6.1 Cryptorchidism

Cryptorchidism, or undescended testes (UDT), is the most common male endocrine gland disorder in children with reported rates from 2 to 8 % in full-term boys and up to 30 % in preterm males [52]. Testicular descent occurs in the seventh month of fetal life and depends on a multitude of factors including activation of gene SRY, appropriate gonadal differentiation, development of the gubernaculum, and a variety of hormones including testosterone and insulin-like hormone 3 (INSL3). Descent occurs in two phases, transabdominal and inguinoscrotal, and is usually complete by the time of birth [53]. Given the multitude of factors involved in testis development and descent, it is not surprising that the pathogenesis is also considered to be multifactorial with both genetic and environmental influences.

12.6.1.1 Definitions

True cryptorchidism can be confused with other entities of abnormal testis position. For clarification purposes, normal scrotal position is the positioning of the midpoint of the testis at or below the midscrotum. The following are descriptions of abnormal scrotal positioning:

- Undescended testis – the absence of one or both testes in a normal scrotal position; may be a palpable or nonpalpable testis
- Vanishing testis – a testis that was lost due to vascular compromise, i.e., torsion, may occur in utero
- Agenesis – the complete absence of testis development
- Secondary/acquired cryptorchidism – testes that are suprascrotal after previous documentation of normal position, such as after inguinal hernia repair
- Retractile testes – testes that are easily manipulated into a normal scrotal position but are usually located in retracted position, such as is seen with an increased cremaster muscle reflex [52]

12.6.1.2 Assessment and Management

Accurate evaluation of the scrotum and testes requires examination in the supine, seated, and upright positions. A warm environment, warm hands, and abduction of the thighs help to decrease elicitation of the cremaster reflex, or testicular elevation due to contraction of the cremaster muscle. Repeated examinations also help to decrease this reflex. Seventy-five to eighty percent of cryptorchid testes are palpable and a majority of cases, reported from 60 to 70 %, are unilateral [52]. Palpable testes are usually present along the line of descent, but may be located in ectopic positions such as perineal, peripenile, lower abdominal wall, or femoral.

In the case of nonpalpable testes, surgical exploration is the gold standard of diagnosis and also allows for definitive management. Ultrasonography, CT, and MRI have been used for diagnosis, but the reported accuracy rates for identification of cryptorchid testes is highest in the inguinal region, which is the most easily palpable undescended testis. Accuracy drops to

less than 50 % when the UDT is in an abdominal location. Therefore, exam under anesthesia and laparoscopic or open exploration provides opportunity for both diagnosis and orchidopexy if a viable testis is found [54].

12.6.2 Hydroceles and Hernias

Development of the processus vaginalis and inguinal canal begins in the third trimester in both sexes, though more prominent development of the processus vaginalis is noted in males to allow transinguinal passage of the testis into the scrotum [55]. The processus becomes obliterated within and just distal to the inguinal canal, then known as the funicular process, but remains patent around the testis to become the tunica vaginalis. Incomplete closure of the processus vaginalis may result in a symptomatic hernia in 1–5 % of newborns or hydrocele in 2–5 % of newborn males [56]. The incidence of hernias and hydroceles is nine times greater in males than in females [57].

12.6.2.1 Hydroceles

Hydroceles present as a spectrum of anatomic varieties depending on the presence and location of processus vaginalis obliteration. The spectrum includes (1) communicating hydrocele with complete patency of the processus vaginalis with passage of intraperitoneal fluid; (2) encysted hydrocele with obliteration proximal to the testis, i.e., spermatic cord hydrocele; and (3) noncommunicating hydroceles that usually occur later in life and are due to accumulation of fluid around the testis with or without a patent processus vaginalis (Fig. 12.6).

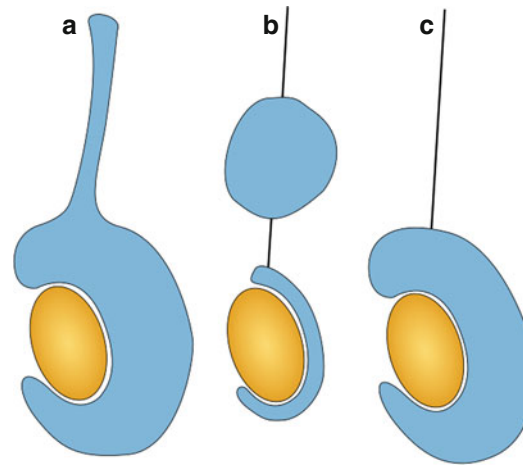

Fig. 12.6 Classification of hydroceles: (**a**) Communicating hydrocele (**b**) Encysted hydrocele or spermatic cord hydrocele (**c**) Noncommunicating hydrocele (Illustration courtesy of David A. Hamilton, Jr., M.D)

Assessment

Most hydroceles present as a painless scrotal or inguinal swelling. Communicating hydroceles are usually fluctuant and may appear larger at the end of the day or with increased activity. Encysted hydroceles of the cord may be confused with an incarcerated inguinal hernia as they appear to be "nonreducible." Rarely is a hydrocele accompanied by pain, so other causes of an acute scrotum must be ruled out. However, in some cases, incarceration of the hydrocele sac can occur with associated symptoms of nausea, vomiting, and fever just as is seen with an incarcerated hernia [58].

Transillumination of the hydrocele classically differentiates it from a hernia, but this is not reliable in infants as a hernia may also transilluminate in bright light. However, if a groin swelling fluctuates with changes in position or stretching of the cord, or if there is a blue coloration to the swelling, this is suggestive of a hydrocele. Hernias are more likely to extend up toward the inguinal canal, are typically reducible, may have palpable crepitus of bowel contents, and may be exacerbated with Valsalva maneuvers.

Management

As most congenital hydroceles resolve spontaneously within the first year of life, conservative management is recommended. Surgical intervention is recommended when the hydrocele persists greater than 12 months or if the hydrocele presents later in childhood.

12.6.2.2 Hernias

The major difference between a hydrocele and a hernia is the size of the opening of the processus vaginalis. If the opening is large enough to allow passage of abdominal viscera in addition to

peritoneal fluid, this is an indirect inguinal hernia. The incidence of inguinal hernias is 1–5 % across both sexes with a male to female ratio as high as 9:1 [55]. There is an increased occurrence of right-sided hernias and unilaterality, and these may occur in up to 30 % of premature infants [55]. Indirect inguinal hernias are the vast majority of pediatric hernias, though direct and femoral hernias can also occur. Indirect and direct inguinal hernias both present as a groin bulge and so must be delineated at the time of surgery. However, a femoral hernia usually presents as an upper or medial thigh bulge. It has been reported that up to 20 % of indirect inguinal hernias are associated with hydroceles [53].

The risk factors for congenital inguinal hernias include having a first-degree relative with history of congenital inguinal hernias, especially if this relative is female. There is overlap of risk factors with cryptorchidism that include low birth weight, bladder exstrophy, cystic fibrosis, connective tissue disorders, epididymal anomalies, and posterior urethral valves [59]. Inguinal hernia is also a component of over 200 syndromes and is more common in patients with ventriculoperitoneal shunts and other disorders causing increased intra-abdominal fluid such as peritoneal dialysis [52].

Assessment

As previously mentioned, inguinal hernias and hydroceles can be clinically difficult to distinguish. An inguinal hernia is typically unique from a hydrocele in that it may extend into and above the inguinal canal and can be elicited by maneuvers that increase intra-abdominal pressure such as crying or laughing. A hernia may also be reducible versus ballotable or fluctuant like a hydrocele. The "silk glove" sign is indicative of a hernia and is elicited by palpating the cord over the pubis that results in a sensation of the layers of the hernia sac slipping over one another [60]. Though not routinely used, ultrasonography of the scrotum and inguinal canal can be used to differentiate inguinal hernia from hydrocele and allows visualization of the testis. Ultrasonography is also useful in determining if an associated condition such as cryptorchidism or testis tumor with secondary hydrocele is present.

An incarcerated hernia is evident by inability to reduce the contents of a known hernia, whereas a strangulated hernia is incarcerated with compromised blood flow resulting in ischemia and necrosis of the hernia contents with associated systemic signs such as nausea, vomiting, fever, and even shock. Incarceration and strangulation are indications for urgent and emergent surgical intervention, respectively. Risks of delayed intervention include bowel necrosis, sepsis, and even death.

Management

Unlike neonatal hydroceles, the rate of spontaneous resolution of indirect inguinal hernias is low. Therefore, elective repair of the defect is recommended with either an open or laparoscopic approach. Cases of incarceration and strangulation are, as previously mentioned, repaired in an urgent or emergent fashion. If associated ipsilateral cryptorchidism is present, delay for observation of spontaneous testicular descent is not recommended; both entities can be surgically corrected in the same procedure.

The traditional inguinal approach for hernia/hydrocele repair is preferred due to its high success rate and low morbidity. There is a 0.7–1 % recurrence rate related to increased hernia size, poor surgical technique, or comorbid conditions that affect wound healing [61]. There is a potential need for later operation in the instance that a persistent or secondary hydrocele occurs without spontaneous resolution. There has been an increase in laparoscopic hernia/hydrocele repairs over the last several years with reported rates of recurrence similar to open approaches with improved pain control [62].

Selective exploration or repair of the contralateral side in cases of unilateral inguinal hernia is a matter of debate as there is no consensus recommendation and current practice varies widely among surgeons [63]. However, with use of laparoscopic technique, it is commonplace to visually inspect the contralateral inguinal ring while repairing a hernia and does not add morbidity to the case as an open contralateral inguinal dissection could.

12.6.3 Varicoceles

12.6.3.1 Etiology

A scrotal varicocele is an abnormal tortuosity and dilatation of the veins of the pampiniform plexus of the spermatic cord. It is a common finding in otherwise normal males but has been linked to subfertility. The exact effect on fertility is unclear as a reported 85 % of men with varicoceles have fathered children [64], yet the incidence in male partners of infertile couples is as high as 30 % [55].

Although varicocele is considered a congenital lesion, it is rarely diagnosed before school age as progression of size and severity is related to increased Tanner stage. The reported incidence in this age group is similar to that reported in adults, ranging from 8 to 16 % [61]. Factors predisposing children to varicoceles include varicocele in a first-degree relative, an ectomorph body habitus, and intrinsic venous abnormalities [65]. Almost 90 % of varicoceles occur on the left side, reflecting the differences in venous anatomy with the left gonadal vein draining into the left renal vein and the right gonadal vein draining directly into the inferior vena cava. Several patterns of intrinsic and anatomic venous abnormalities have been described:

- Incompetency or absence of valves
- Anomalous venous drainage, i.e., between gonadal and retroperitoneal veins
- Abnormal point of entry of gonadal vein into the left renal vein with resultant turbulent/decreased flow

12.6.3.2 Assessment and Classification

Varicoceles are typically detected during routine examination or the patient may present with scrotal swelling or discomfort. The typical description of the exam finding is that of a "bag of worms" in the scrotum. The standard grading system is as follows:

- Subclinical – neither palpable nor visible but detectable by Doppler ultrasonography
- Grade I – palpable only with Valsalva maneuver
- Grade II – palpable at rest but not visible
- Grade III – palpable and visible at rest

12.6.3.3 Associated Pathology

The presence of a varicocele is associated with an increase in scrotal temperature that may be related to altered testicular growth, spermatogenesis, and semen quality [66]. These relationships are unclear, however, as definite links between these parameters and fertility have not been clearly established. Some specifically reported abnormalities include testicular hypotrophy, abnormal tubular maturation or tubular degeneration, altered Leydig cell number, exaggerated LH and FSH response to GnRH, and poor semen quality [63]. Interestingly, higher varicocele grade has not been definitively linked to inferior semen parameters [65].

12.6.3.4 Management

Despite the unclear link between the pathologic findings associated with varicocele in adolescence and potential for later reproductive ability, the current indications for surgical intervention are pain and significant hypotrophy of one or both testes in infants, with the additional indication of improving fertility in teenagers and adults [65].

There are various approaches to surgical intervention including microsurgical varicocelectomy, laparoscopic or open varicocelectomy, and sclerotherapy or embolization with the common goal of ligation of venous outflow. Laparoscopic and microsurgical approaches are associated with the lowest incidence of both recurrence and hydrocele, especially when employing lymphatic-sparing techniques [64].

12.6.4 Testicular Torsion

The sudden onset of swelling, pain, and/or tenderness of the scrotum or scrotal contents is referred to as an "acute scrotum." Testicular torsion accounts for 80–90 % of male patients' age 13–21 presenting with an acute scrotum. There is a bimodal distribution of torsion with peaks within the first year of life and in early adolescence with an overall incidence of 3.8 per 100,000 [67]. An extensive differential diagnosis of causes of the acute scrotum exists,

but testicular or spermatic cord torsion is a surgical emergency and requires intervention within 6 h of onset to avoid long-term sequelae related to reduction or cessation of blood flow to the testis.

Spermatic cord or testicular torsion occurs in one of two ways: intravaginal or extravaginal. Intravaginal spermatic cord torsion occurs when the testis twists within the tunica vaginalis. This is more common in teenage boys and is predisposed by the bell-clapper deformity in which the tunica completely or partially fails to fuse to the epididymis, allowing incomplete attachment of testis/epididymis to the scrotum. Bell-clapper deformity was identified in 12 % of males in an autopsy series, but torsion occurs at a much lower incidence of 0.009 % [68]. The inciting event is unknown in most patients but may include cold temperature, sudden movement, trauma, or rapid growth of the testis at puberty.

Extravaginal torsion occurs most commonly in the perinatal period. This is due to rotation of the entire cord, testis, and tunica vaginalis before the fixation has been established between the dartos and the tunica vaginalis. This is more common while the patient remains in utero, but has also been described at several months of age. We will focus the further attention of this section on perinatal, or extravaginal, torsion.

12.6.4.1 Etiology and Assessment

Postulated risk factors include large birth weight, difficult delivery, or a family history of torsion [69]. Typical exam findings include induration of the scrotal skin or testis and scrotal edema, erythema, and/or discoloration. Patients may present with pain, but are usually asymptomatic making timely diagnosis difficult. Hydroceles may coexist, further complicating accurate diagnosis.

Ultrasound is the imaging modality of choice to diagnose torsion, especially with the use of Doppler to detect vascular flow. Sensitivity and specificity for accurately diagnosing torsion are reported as high as 100 and 95 %, respectively, in some series [70]. If, however, imaging is nondiagnostic, surgical exploration is advocated in lieu of delaying or avoiding treatment.

12.6.4.2 Management

Most cases of extravaginal torsion are not salvageable as they occur during the prenatal period while the fetus remains in utero. However, partial or complete salvage is possible in some cases if emergent surgery is performed; this is the most prudent approach to minimize loss of testicular tissue. Contralateral exploration and orchidopexy should be performed at the same time as emergent detorsion/orchidopexy.

12.7 Disorders of Sex Development

Disorders of sex development (DSD), previously known as intersex disorders, are due to one of the following mechanisms: chromosomal defects, abnormal gonadal development, or defects in sex hormone production or sex hormone receptors. These infants present at birth with ambiguous genitalia. Associated medical conditions such as congenital adrenal hyperplasia and adrenal insufficiency may also be present and require urgent intervention. In the cases when an urgent underlying medical condition is not present, disorders of sex development warrant a thorough investigation from a multidisciplinary team including a pediatric endocrinologist, a pediatric urologist, a radiologist, and a geneticist. Support and counseling for the parents should also be available, and assignment or registration of gender should be delayed until a formal diagnosis has been made [71].

12.7.1 Normal Sexual Differentiation

Precursors of gonads and external genitalia are present in an identical state in both 46XX and 46XY embryos until gestational week 6. Development down a phenotypic female pathway occurs passively unless the presence of certain genes and hormones activates male differentiation. In this case, the presence of *SRY* (sex-determining region Y) on the Y chromosome in addition to secretion of Mullerian inhibitory substance (MIS) and testosterone is responsible

Table 12.1 Revised nomenclature for disorders of sex development (DSD)

Previous nomenclature	Current nomenclature	Presentation
Intersex	Disorders of sex Development (DSD)	(See below)
Female pseudohermaphrodite	46 XX DSD	Virilization of 46XX fetus
Male pseudohermaphrodite	46XY DSD	Incomplete virilization of 46XY fetus
True Hermaphrodite	Ovotesticular DSD	Both ovary and testis present; variable genotype and phenotype
Gonadal dysgenesis	Gonadal dysgenesis (unchanged)	Loss of one pair of sex chromosomes, e.g., 45X or 45X/46XY; variable genotype and phenotype

for the early development of male internal and external genitalia with regression of female characteristics [72].

12.7.2 Classification

As previously mentioned, the origin of DSD can be chromosomal defects, abnormal gonadal development, or endocrine dysfunction. The most commonly seen forms of DSD are as follows (see Table 12.1):

- 46XX DSD – virilization of a 46XX fetus due to exposure to virilizing agents such as testosterone
- 46XY DSD – incomplete virilization of a 46XY fetus
- Ovotesticular DSD – both ovarian and testicular tissue are present; phenotype and genotype are highly variable
- Gonadal dysgenesis – a spectrum of gonadal and genital abnormalities that occurs due to the loss of one of a pair of sex chromosomes, e.g., 45X or 45X/46XY mosaicism

12.7.2.1 46XX DSD

46XX DSD is composed almost entirely of 46XX females with normal gonads and internal genitalia but ambiguous external genitalia. Congenital adrenal hyperplasia is by far the most common cause of 46XX DSD and accounts for a vast majority of cases of ambiguous genitalia in the West. This disorder can result from one of three enzymatic defects in the pathway for adrenal production of cortisol and aldosterone that in turn causes increased adrenocorticotropic hormone (ACTH) production with resultant overproduction of androgens (see Fig. 12.7). The most common defect is 21-hydroxylase deficiency that results in elevated 17α-hydroxyprogesterone and can be associated with life-threatening hyponatremia. 11ß-hydroxylase deficiency is associated with hypernatremia, hypokalemia, and severe virilization. 3ß-hydroxysteroid dehydrogenase deficiency is the least common of the three defects and is similar to 21-hydroxylase deficiency but with less severe virilization [72, 73, 76].

Prenatal diagnosis is possible, and suppression of ACTH with dexamethasone has been successfully reported in cases. However, if diagnosis is made at birth, management includes replacement of necessary substrates, management of electrolyte imbalances, and female assignment with feminizing genitoplasty if indicated [73–75].

Less common causes of 46XX DSD include deficiency of estrogen synthetase that normally synthesizes estrogens from androgen precursors and exposure of the fetus to maternal androgens from androgen secreting tumors of the adrenals or ovaries.

12.7.2.2 46XY DSD

Male infants with 46XY DSD exhibit varying degrees of incomplete virilization due to defects in androgen production and metabolism or defective androgen receptors. Defective testosterone production is rare, but may be due to testicular dysgenesis or an enzymatic defect in the biosynthetic pathway. Testosterone conversion to its more potent form dihydrotestosterone (DHT) is regulated by the enzyme 5α-reductase. A deficiency in this enzyme is most common in consanguine communities in the Dominican Republic and may appear to be normal phenotypic

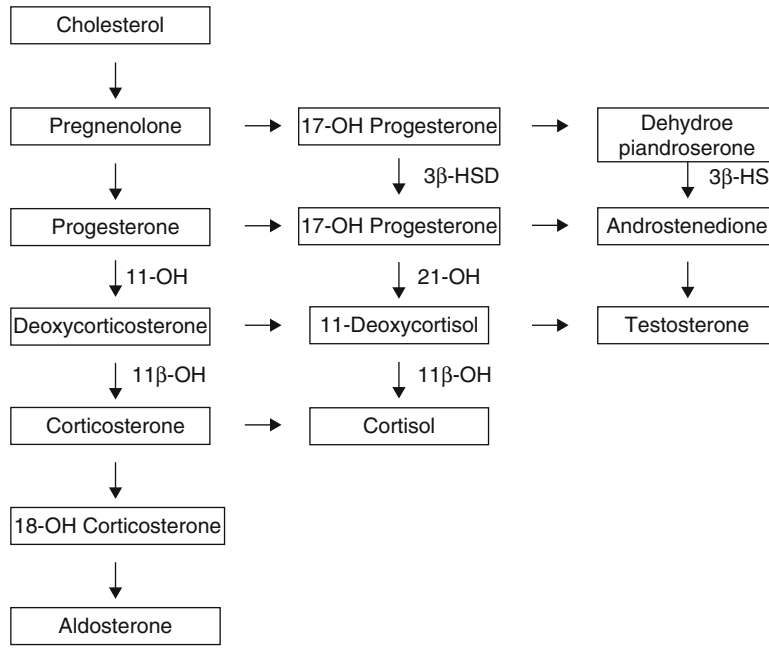

Fig. 12.7 Sites of enzyme deficiency in congenital adrenal hyperplasia

females until virilization occurs at puberty with increased levels of testosterone that overcome the DHT deficiency [74, 76].

Androgen insensitivity syndrome is characterized by tissue resistance to testosterone with resultant female phenotypic external genitalia. However, the presence of MIS still drives internal genitalia and gonadal differentiation down a normal male pathway. This condition is usually discovered when investigating causes of primary amenorrhea or if a testis is found during herniorrhaphy in a female patient. On the other hand, MIS deficiency or MIS receptor insensitivity results in normal male external genitalia with persistent Mullerian structures [74].

12.7.2.3 Gonadal Dysgenesis

Dysgenesis or abnormality of the development of the gonads can lead to a variety of genotypic and phenotypic presentations depending on the presence of any normal functioning gonadal tissue. For example, a 45XO (Turner syndrome) female will have normal female internal and external genitalia since no tissue with a Y chromosome is present. However, mixed gonadal dysgenesis with 45X/46XY mosaicism results in a broad spectrum of gonadal and external phenotypes due to the presence of both X and Y chromosomes with incomplete function of the dysgenetic gonads with an associated increase in malignancy risk in these gonads [74].

12.7.2.4 Ovotesticular DSD

Previously known as true hermaphroditism, ovotesticular DSD is a variation of gonadal dysgenesis in which both testicular and ovarian tissue are present in an individual, and in some cases, within the same gonad. The external genitalia are invariably ambiguous. This is virtually a diagnosis of exclusion and sometimes relies on macroscopic or microscopic examination of the gonads. Gender assignment proves difficult in this population and usually requires hormone supplementation and surgical reconstruction [75].

12.7.3 Assessment

Evaluation of neonates with ambiguous genitalia should include a physical exam that focuses on the degree of virilization, the presence of palpable gonads, and identification of other congenital abnormalities. History should include details of the pregnancy as well as a thorough

family history with attention to any defects present in siblings [75].

Initial laboratory evaluations should include karyotype, serum electrolytes, and 17-hydorxyprogesterone levels. A more detailed evaluation might include a steroid assay, serum testosterone levels, MIS levels, and even DNA analysis to identify specific gene mutations [77].

Diagnostic imaging is useful for identifying gonads or internal genitalia via ultrasonography. Ultrasound is the primary modality for imaging internal organs. Genitograms, or contrast studies performed through a catheter placed into the urethra, vagina, or opening of the urogenital sinus, are helpful to determine the presence of internal genitalia such as the uterus, fallopian tubes, or even the vasa deferentia [78].

Direct visualization via surgical methods is sometimes indicated. Endoscopy of the lower genitourinary tract, such as vaginoscopy or cystourethroscopy, and laparoscopy are useful minimally invasive procedures. However, there is still an indication for laparotomy in some instances when identification of the gonads and/or biopsy of gonads is not possible through less invasive means [75, 77].

12.7.4 Management

After medical stabilization of the patient when indicated, the next most important step in management of a child with DSD is gender assignment. This should be delayed until a formal diagnosis has been established. Each case must be tailored to the patient's particular features including genital appearance, fertility potential, familial or cultural preferences, and surgical and/or medical requirements.

Female assignment is almost invariably advised in cases of 46XX DSD as most patients have normal female internal genitalia and gonads. Female gender assignment is also often advised in cases of 46XY DSD with the exception of those patients that have a positive response to androgen stimulation. In mixed gonadal dysgenesis and ovotesticular DSD, gender assignment is variable but usually depends on the presence of functional gonadal tissue. Female assignment is more common for this group unless sufficient androgen response and external male genitalia is present, though practice varies widely among practitioners. Orchidopexy in patients assigned male gender is necessary to enable examination of the testes, and orchiectomy in patients assigned female gender is advised given the increased risk of malignancy in these gonads [79, 80].

Once gender assignment has been completed, hormonal and surgical therapy can then be pursued. As previously mentioned, a multidisciplinary team including pediatric endocrinology, pediatric urology, radiology, genetics, and psychiatry/counseling for the parents is often necessary to address all aspects of management of these children.

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