Congenital urogenital malformations

Congenital abnormalities of the kidney and urinary tract are one of the most frequent major birth defects, representing up to 20-30% of all major birth defects.[1]

Congenital anomalies of the kidney and urogenital system range from mild, asymptomatic malformations to severe, life-threatening pathologies and complex ethical dilemmas.

Many congenital abnormalities are part of a syndrome whose impact extends beyond the urogenital system - for example, there are some congenital urological abnormalities leading to oligohydramnios and, therefore, severe pulmonary problems.

Sometimes treatment is possible, including treatment in utero. Advances in prenatal diagnosis, fetal surgery and targeted therapies have improved the prognosis and quality of life in affected families.[2]

Congenital abnormalities of the kidney[2]

The kidney is the most common site of congenital abnormalities. Some cause no problems but many result in impaired renal function. Renal malformations are often associated with other congenital defects.

Renal agenesis

- Virtually always unilateral (1 in 1,000 to 1 in 2,000 births). Bilateral renal agenesis is incompatible with life.
- Renal agenesis and severe renal dysplasia are also termed hereditary renal adysplasia. The kidney is either absent or undeveloped.
- One absent kidney usually causes no symptoms and is found incidentally.

- It is thought to be an autosomal dominant trait with incomplete penetrance and variable expression.
- Ultrasound study of the kidneys of parents and siblings is recommended in all families with an affected individual.[3]
- There is a compensatory increase in glomerular filtration in the single kidney. Theoretically this could lead to progressive damage to the remaining renal tissue, generating hypertension if unresolved, although studies suggest that renal function remains stable for several decades in most subjects.[4]
- The clinical significance of mild-grade proteinuria and hypertension seen in some patients is unknown.[4]
- Unilateral renal agenesis (URA) can be associated with other congenital anomalies of the kidney and urinary tract (CAKUT) and extra-renal anomalies. In one systematic review, CAKUT were present in around a third of patients, most commonly vesicoureteral reflux. Extra-renal anomalies were also found in around a third. Hypertension was identified in 16% of patients, 21% of patients had micro-albuminuria and 10% of patients had GFR <60.[5]

Renal dysplasia and multicystic kidney

Renal dysplasia is described as a developmental disorder where the kidneys fail to differentiate normally, resulting in the presence of primitive tubules, interstitial fibrosis, renal cysts and cartilage in the renal parenchyma.[6]

- Multicystic kidney of the newborn is normally seen in only one kidney as an irregularly lobulated mass of cysts and usually absent or atretic ureter.
- Frequently associated with contralateral abnormalities, especially ureteropelvic junction (UPJ) obstruction.
- 60% of kidneys affected by renal dysplasia have an obstructive component.[2]
- Dysplasia of the renal parenchyma is seen with urethral obstruction or reflux present early in pregnancy, or obstructed ureter.

Potter's syndrome

- Potter's syndrome occurs in sporadic and autosomal recessive forms with an incidence of 1 in 4,000 births.
- The name describes the typical physical appearance caused by oligohydramnios. This is classically due to bilateral renal agenesis (BRA), although it can occur with other conditions, including infantile polycystic kidney disease (IPKD), renal hypoplasia and obstructive uropathy.
- Oligohydramnios leads to pulmonary agenesis (usually with fatal outcome) and characteristic facies (folds under the eyes, flat nose, low-set ears and a receding chin).
- Bilateral renal agenesis is incompatible with life.[7]
- In the past the condition often led to caesarean section, as it was usually associated with premature delivery, and breech presentation is a frequent finding. Prenatal ultrasound diagnosis of BRA can avoid unnecessary surgery to the mother.[8]

Renal hypoplasia

Renal hypoplasia is defined as a more marked reduction in renal mass such that presentation is usually in childhood. There are three commonly recognised types of renal hypoplasia: simple hypoplasia, oligomeganephronic hypoplasia (oligomeganephronia) and segmental hypoplasia. They all have a reduction in the number of renal lobes.[9]

- There may be one small kidney with the other one larger than normal, or both may be smaller.
- Minor degrees of unilateral renal hypoplasia are common and, generally, asymptomatic.
- The condition differs from renal dysplasia in that the kidneys are otherwise morphologically normal. There is normal residual parenchyma but smaller calyces, lobules and papillae.
- Small kidneys also have small renal arteries and are associated with hypertension requiring nephrectomy.
- Segmental renal hypoplasia, also known as the Ask-Upmark kidney, is associated with severe juvenile hypotension. It can be either congenital or the result of pyelonephritic insult in childhood.[10]

Supernumerary kidneys

- Third kidney is extremely rare and not to be confused with the relatively common unilateral duplication of the renal pelvis.
- It may be found incidentally or during investigation of other anomalies.
- Fewer than 100 cases have ever been reported - even fewer of bilateral supernumerary kidney.
- They are more commonly on the left.
- Ureteric drainage systems to the extra kidney vary but additional ureteric and genital abnormalities are typical and hydronephrosis is common.[11]

Polycystic kidney disease

Adult polycystic kidney disease (APKD)[2]

- APKD affects 1 of every 400-1,000 live births and accounts for approximately 10% of patients with chronic kidney disease requiring dialysis or transplant.
- This is a systemic disorder that mainly affects adult patients. They also develop hepatic and pancreatic cysts, chronic hypertension, intracranial aneurysms and cardiac valve anomalies - especially mitral valve prolapse.
- The likelihood of severe renal disease increases progressively with age.

Infantile polycystic kidney disease (IPKD)[2]

- IPKD has an incidence of 1 in 20,000 to 1 in 40,000 live births and a heterozygous carrier rate of the responsible gene of 1 in 70 (homozygous recessive).
- Severely affected fetuses are born with oligohydramnios and Potter facies; some will develop respiratory insufficiency.
- Approximately 40% have severe hepatic and renal disease, 30% have severe renal and mild hepatobiliary disease and the other 30% have severe hepatobiliary problems and mild renal disease.

- The condition is always bilateral. The hepatic manifestation is of congenital hepatic fibrosis, leading to portal hypertension.

Simple (solitary) renal cyst[12]

- This may be inherited or acquired.
- Significant renal damage is rare and usually only requires continuous follow-up.
- The prevalence of renal cysts increases with age.
- They are twice as common in men as they are in women.
- Renal cysts progress in size and number and appear to grow more rapidly in younger patients.

Renal fusion (horseshoe kidney)

Horseshoe kidney is the most common renal fusion anomaly, with a prevalence of 0.25% among the general population. It consists of kidney fusion across the midline.[13]

- Most are fused at the lower pole.
- Fusion is twice as common in males as it is in females. It is usually associated with a narrow pelvis as seen in trisomy 18.
- Most fused kidneys are positioned lower than normal. The central part of the horseshoe is just below the inferior mesenteric artery, as the normal embryological ascent is arrested by its presence.
- Prevalence is around 1 in 600 people.[14]
- The most frequent abnormality seen is a horseshoe kidney containing two excretory systems and two ureters.
- Patients are prone to a variety of complications, such as stone disease, PUJ obstruction, trauma, infections and tumours.
- As a result of the abnormal anatomy of a horseshoe kidney, imaging and treatment pathways vary substantially from those for the normal kidney.[15]
- Children can present with urinary tract infections (UTIs), abdominal mass and haematuria.

Ectopic kidney [16]

- In simple ectopy, the kidney does not ascend properly and is found in the pelvis or over the brim.
- The ureter of a pelvic kidney is tortuous. Ureteropelvic junction (UPJ) obstruction occurs in around 30%.
- The pelvic kidney is prone to obstruction, calculi and infection.
- The incidence is 1 in 2,200 and 1 in 3,000.
- A nonfunctional pelvic kidney may require removal.
- Less common than the pelvic kidney are crossed ectopy without fusion (ie the two kidneys are completely independent but on the same side) and abnormal rotation of the kidney. These are usually incidental findings which rarely lead to renal disease.

Medullary sponge kidney (MSK) [17]

- MSK is seen in 1 in 5,000 to 1 in 20,000 people.
- There is cystic dilatation of the collecting tubules in one or both kidneys.
- Nephrocalcinosis and recurrent renal stones are usually seen. Affected women experience more stones, UTIs and complications than men experience.
- MSK is generally considered a sporadic disorder but an autosomal dominant inheritance has also been observed.
- There are often other associated urinary tract developmental anomalies.

Trisomies and congenital anomalies of the kidneys

Renal anomalies are not a constant feature of trisomies; however, in the literature numerous examples have been reported of children with trisomies 13, 18 and 21 who also have hydronephrosis, horseshoe kidney, duplex kidney/collecting system, cortical cysts and/or cystic dysplasia, glomerular microcysts, or renal hypoplasia. [3]

Abnormalities of the ureter and ureteropelvic junction [2] [18]

Ureteral duplication may be incomplete or complete. Incomplete duplication is also known as a bifid collecting system.

Ureteral atresia [19]

- The ureter may be absent or fail to extend to the bladder (therefore, with a blind ending).
- It is a rare condition, associated with ipsilateral absent or multicystic kidney.
- Ureteral atresia is a rare congenital abnormality usually associated with a dysplastic non-functioning kidney. It may present with hydronephrosis detected during prenatal ultrasound.
- It is thought to be caused by a failure of canalisation of a segment of ureter during the process of development and elongation of the ureteric bud.
- Bilateral atresia is incompatible with life. Unilateral atresia is usually asymptomatic but may cause hypertension.

Duplication of the ureter [20]

- This is one of the most common congenital malformations of the urinary tract, with duplication found in 0.9% of a series of autopsies.
- Duplication may be either complete or incomplete and is often accompanied by various complications.
- Incomplete duplication is most often associated with ureteral reflux or UPJ obstruction of the lower pole of the kidney.
- Complete duplication is most often associated with vesicoureteral reflux, ectopic ureterocele, or ectopic ureteral insertion, all of which are more common in girls than in boys.
- It is often bilateral.

- If there are two separate pelvicalyceal systems joined at the UPJ, this is considered a bifid pelvis; if there are two separate ureters proximally and they join at any point below the UPJ but before entering into the bladder, the patient is considered to have bifid ureters. Complete ureteral duplication occurs when there are two separate ureters that continue and enter the urinary bladder .
- If obstruction is maintained for some time, the kidney can become hydronephrotic. Persistent infection can lead to chronic pyelonephritis and to chronic renal disease.
- Most cases are asymptomatic in adults; in children the risk of renal infection is increased 20-fold.
- The mode of inheritance is autosomal dominant.
- Conjoint ureter is more common than complete ureteral duplication. If one of the two parts ends blindly, it is named a congenital ureteral diverticulum. Double ureter is more common in girls than in boys in a ratio of 6:1.

Ureterocele [21]

- This is a sacculation of the bladder end of the ureter that can occur either in the bladder or ectopically.
- It is much more common in girls than in boys.
- In 10% of cases it is bilateral.
- It may be asymptomatic or be associated with vesicoureteral reflux and/or obstruction of the bladder outlet. [22]
- Ureteroceles are infrequently seen.

Ectopic ureter [23]

- This usually occurs with ureterocele and duplication of the ureter but single ectopic ureters are seen.
- Boys may present with epididymitis, as the ureter drains directly into the vas deferens or seminal vesicle.
- Girls may have urinary incontinence with persistent dribbling when the ectopic ureter opens into the urethra distal to the sphincter.

Obstruction of the UPJ [24]

- UPJ obstruction describes various causes of impaired drainage at the UPJ. The most common is a kink in the ureter where it meets the dilated renal pelvis.
- UPJ obstruction has an incidence of 1 in 1,000 to 1 in 1,500 newborns and is the most common cause of antenatal hydronephrosis.
- There are many causes, including insertion anomalies of the ureters, ureteral muscular hypertrophy, peri-pelvicalyceal fibrosis, and abnormal blood vessels crossing over the ureter or renal pelvis.
- Long-standing obstruction may lead to pyelonephritis, hydronephrosis and chronic renal disease.
- It can be diagnosed in utero.
- It results in the impedance of urine flow from the renal pelvis into the proximal ureter, resulting in caliectasis and hydronephrosis, leading to to progressive deterioration of renal function.
- It accounts for 80% of all dilated collecting systems identified antenatally by fetal ultrasonography.
- In children, it normally presents with pain and vomiting.
- A significant number will require intervention - some do not present with functional obstruction until adulthood.
- Male-to-female predominance is greater than 2:1; the left kidney is affected about twice as often as the right.
- Acquired stenosis of the UPJ can also occur after UTI, stones, trauma, ischaemia or extrinsic compression.

Prune belly syndrome (PBS) [25]

- This is very rare: PBS affects 3.8 per 100,000 live male births.
- The classical triad is of urinary tract anomalies, deficient abdominal musculature, and bilateral cryptorchidism.

- There is oligohydramnios, bilateral hydronephrosis, and obstructive renal dysplasia. The bladder is greatly distended, leading to failure of the muscle layer to develop. There is undescended testis and intestinal malrotation as the distended bladder does not allow normal positioning of either.
- After drainage, the abdomen wrinkles and acquires the appearance of a prune, hence the name.
- It is associated with a broad spectrum of defects such as club foot, pulmonary hypoplasia, Potter facies, imperforate anus and arthrogryposis. Most have malformations of cardiopulmonary, gastrointestinal and orthopaedic systems.
- The aetiology is not known.
- The bladder can be drained in utero, preventing oligohydramnios syndromes and the prune belly. However, many infants are stillborn or die within weeks.
- 96% of those affected are male.
- A few affected people have survived into adult life after abdominal reconstruction and urinary tract repair.

Obstructed mega ureter[26]

- This is caused by obstruction at the ureterovesical junction.
- It is four times more common in boys than in girls and is often bilateral.
- Often, it is associated with absent or dysplastic contralateral kidney.
- It is usually discovered during prenatal ultrasound.
- It frequently presents with haematuria, with symptoms of infection and abdominal pain.

Abnormalities of the bladder[18]

Bladder exstrophy

- This is absence of the anterior wall of the bladder, with ureters delivering urine into the lower abdomen.

- It is associated with other abnormalities, especially epispadias.
- It requires surgical reconstruction.
- Bladder exstrophy and classic epispadias lie on a spectrum of congenital anomalies with different degrees of anterior midline defect. Although they usually occur sporadically, there can sometimes be a genetic component.[27]

Persistent urachus

This may appear as a draining umbilical sinus and can become infected.

Contracture of the bladder neck

This is a common cause of reflux, bladder diverticula and irritable bladder.

Anomalies of the penis and urethra in males[18]

Penis agenesis (aphallia)[28]

- Aphallia is an extremely rare disorder with profound urological and psychological consequences.
- More than 50% of patients have associated genitourinary anomalies - eg, cryptorchidism, renal agenesis and dysplasia.
- In addition to correction of life-threatening anomalies, the management centres on establishing gender assignment. Bilateral orchiectomy, labial construction and urethral transposition can be done in the newborn period.

Megalophallus

The penis enlarges rapidly in childhood, due to a high level of production of testosterone.

Micropenis

This is a small but otherwise normally formed penis with a stretched length of less than 2.5 standard deviation below the mean. It is important to distinguish micropenis from buried and webbed penis, which is usually of normal size. The most common aetiologies are:

- Hypogonadotropic hypogonadism: impaired secretion of gonadotrophin-releasing hormone (GnRH) by the hypothalamus occurs in some hypothalamic dysfunctions - eg, Kallmann's syndrome, Prader-Willi syndrome.
- Hypergonadotropic hypogonadism: the testes are functionally impaired - eg, gonadal dysgenesis.
- Idiopathic micropenis: there is normal hypothalamic-pituitary-testicular endocrine function.

Urethral stricture

- This is uncommon; the two most common sites are the fossa navicularis and the membranous urethra.
- Severe cases can result in damage to the bladder and in hydronephrosis due to back pressure of urine.

Posterior urethral valves (PUVs) [29]

- PUVs are the most common cause of lower urinary tract obstruction in male infants and fetuses. They are usually diagnosed prenatally.
- They are seen more often in boys than in girls. Most cases are unilateral and usually on the left.
- They are found at the distal prostatic urethra and mucosal folds, looking like thin membranes and causing varying degrees of obstruction when urination is attempted.
- Boys usually present with a poor, intermittent, dribbling stream with frequent infection.
- PUV is a significant cause of paediatric morbidity, mortality, ongoing renal damage and end-stage kidney disease.
- There is a spectrum of severity depending on the configuration of the obstructive membrane.
- The decision to intervene prenatally is dependent on gestational age, amniotic volume and renal function. Endoscopic ablation of the valve is the gold standard of treatment.

- The ultimate goal of management is to maximise renal function, maintain normal bladder function, minimise morbidity and prevent iatrogenic problems.

Hypospadias [30]

- In hypospadias the urethral opening is not at the usual location on the head of the penis but is below it.
- In 90% of cases, the meatus is on or near the glans (distal hypospadias).
- In the remainder the meatus is near or within the scrotum (proximal hypospadias).
- In most cases the foreskin is defective on the underside of the glans.
- Downward bending of the penis is found in 10% of distal hypospadias and 50% of proximal hypospadias. The scrotum may be higher than usual.
- Hypospadias is thought to result from failure of the urinary channel to tubularise completely. The cause is not known.
- Associated abnormalities are common, most often an undescended testis (10%). This combination can suggest a disorder of sexual differentiation.
- The prevalence has a large geographical variation: recent studies have suggested that reports of both increasing and decreasing temporal trends are incorrect. Overall incidence is around 18 per 10,000 live births.
- There is an association with very low birth weight.
- Young children seldom report symptoms but older children and adults may complain of difficulty in directing the urinary stream and of spraying.
- 9-15% of cases have an open processus vaginalis or inguinal hernia.
- 7% have an additional family member with hypospadias.

Epispadias [31]

- This consists of a defect of the dorsal wall of the urethra so that it ends as an opening on the upper (dorsal) side of the penis.
- It is not a variant of the same process as hypospadias but a completely different embryological defect.
- It can also occur in girls when the urethra develops too anteriorly.
- The extent of the defect can vary from a mild glandular defect to complete defects, as are observed in bladder exstrophy and/or diastasis of the pubic bones.
- Epispadias occurs in 1 in 120,000 males and 1 in 450,000 females.
- The urethra is displaced dorsally so that it opens on to the top of the penis in males.
- Females have a bifid clitoris and separation of the labia.
- Male patients demonstrate a dorsal chordee (bend to the penile shaft).
- Incontinence is a common problem.
- The goal of surgical correction is the placement of the meatus in its anatomical position and the creation of functional genitalia with good cosmetic outcomes.

Anomalies of the testis [18]

Hypogonadism [32]

- Small testes with lack of development of secondary sexual characteristics, lack of libido and potency.
- Characteristically, patients are tall with long extremities.
- It is also associated with Klinefelter's syndrome and undescended testes.
- It is also associated with physiological problems and low intelligence.

Ectopic testis [18]

Ectopy

The testis has not followed the normal path of descent and is located away from it. It is not incomplete descent but maldescent. It is a rare condition and includes individuals in whom both testes are located in the same inguinal region. The ectopic testis may be:

- In the lower abdomen, front of thigh, femoral canal, penile skin or behind the scrotum.
- It is usually developed and there is usually an indirect inguinal hernia.
- The testis may be divorced from the epididymis which may lie in the scrotum.

Cryptorchidism [33]

- Testicular descent is arrested.
- This is the most common congenital anomaly affecting the genitalia of newborn male infants.
- Cryptorchidism is a very common anomaly of the male genitalia, affecting 2-4% of male infants; it is more common in premature infants.
- The exact cause is uncertain.
- The most useful classification is into palpable and non-palpable testes. Clinical management is decided by the location and presence of the testes:
    - Retractile testes require only observation.
    - Bilateral, non-palpable testes and any suggestion of sexual differentiation problems (eg, hypospadias) require urgent, mandatory endocrinological and genetic evaluation.
- The recommended timing for orchidopexy is between 6-12 months of life, in an effort to preserve the spermatogonia - the stem cells for subsequent spermatogenesis.
- Even after orchidopexy, the long-term outcome is problematic. Impaired fertility (33% in unilateral cases and 66% in bilateral undescended testes) and a cancer risk 5-10 times greater are observed.

- Noonan's syndrome occurs in 1 in 1,000 to 1 in 2,500 live births. It can affect either sex and is characterised by multiple abnormalities, including congenital heart disease, short stature, developmental delay, cryptorchidism in boys, increased bleeding tendency and characteristic facial features.

Spermatocele

- This is a painless cystic mass found just above or posterior to the testis.
- They are mostly <1 cm in diameter and usually require no therapy.

Varicocele

- Varicoceles develop slowly and are present at birth. They develop very slowly, are unusual in boys aged under 10 years and are more frequent at the beginning of puberty. (They occur in around 14-20% of adolescents.)
- However, the cause of varicoceles may be congenital absence of valves in the left testicular vein, or the presence of anomalous branches or other abnormal variants of venous drainage.
- They appear mostly on the left side (78-93% of cases). (A unilateral right-sided varicocele is very rare and can indicate obstruction of the inferior vena cava.)
- They are caused by dilatation of the pampiniform plexus (spermatic venous plexus).
- Fertility problems arise in around 20% of adolescents with a varicocele.
- Surgery is recommended for:
    - Varicocele associated with a small testis.
    - Additional testicular condition affecting fertility.
    - Pathological sperm quality (in older adolescents).
    - Bilateral palpable varicocele.
    - Symptomatic varicocele.

Hydrocele[34]

- A hydrocele is a collection of fluid in the scrotum, not associated with an obvious inguinal hernia.
- The typical hydrocele is observed at birth as a unilateral or bilateral swelling in the scrotum, which may fluctuate in size.
- It may be very tense, is usually non-tender and is, often, bluish in colour. Most hydroceles will transilluminate; a fluid- or gas-filled bowel may transilluminate too.
- Most resolve spontaneously by the age of 24 months. Hydroceles that persist beyond that age are unlikely to resolve spontaneously and should, therefore, undergo elective surgical repair.
- Early surgery is indicated if there is suspicion of a concomitant inguinal hernia or underlying testicular pathology.

Female genital anomalies

Distal urethral stenosis[35]

- There is little literature on this condition. It occurs in young girls with enuresis with slow and interrupted stream and recurrent urinary infection. It is thought to be due to congenital distal urethral stenosis with secondary spasm of the striated external sphincter rather than bladder neck obstruction, as previously thought.
- In addition to recurrent UTIs, the girls have a slow, hesitant, or interrupted urinary stream. Enuresis and involuntary loss of urine during the day are common complaints. Abdominal straining may be required in order to void. Small amounts of residual urine may impair the vesical defense mechanism.
- The condition is relieved by urethral dilatation.

Labial fusion[36]

- Fused labia minora can present with recurring urinary infection as a result of obstruction to the urine flow.

- Partial virilisation at birth of a genotypical female can result in varying degrees of posterior labial fusion and clitoral enlargement. It is most commonly due to excess androgen production from congenital adrenal hyperplasia. Rarely, it arises secondary to maternal androgen ingestion or an androgen-secreting tumour during pregnancy.

Clitoral hypertrophy [36]

- This is caused also by fetal exposure to androgens, usually caused by congenital deficiencies of adrenal enzymes of cortisol synthesis.
- Rarely, it may also be due to in-utero exposure to progestational agents or idiopathic virilisation.

Vaginal and uterine anomalies [37]

- Congenital malformations of the vagina, cervix and uterus, although rare, may have profound implications for the young gynaecological patient.
- These anomalies are often detected in the adolescent period. Genital malformations can be particularly disturbing to the patient and her family because they not only have reproductive implications but also significant psychological and sexual and gender identity overtones.
- A range of developmental defects including agenesis, atresia and septation of the reproductive tract, many of which have been associated with genetic syndromes, has been documented.
- Other anomalies often co-exist, particularly related to the renal tract.

Vaginal atresia [38]

- Vaginal atresia is a rare condition, occurring in 1 in 4,000 to 1 in 10,000 females.
- Vaginal atresia is most often characterised by absence of the hymen and occasionally by absence of the vagina extending to the cervix. Cervix, uterus and oviducts are usually normal but the vagina is replaced by fibrous tissue.

- Hydrometrocolpos, a fluid-filled dilated vagina and uterus, can be caused by obstruction from vaginal atresia, transverse vaginal septa, or an imperforate hymen.
- There are several genetic syndromes that have been identified with vaginal atresia as a commonly associated malformation. McKusick-Kaufman syndrome (MKKS) and Bardet-Biedl syndrome (BBS) are two autosomal recessive syndromes with significant overlap which have been associated with vaginal agenesis.

Gonadal dysgenesis[39] [40]

Gonadal dysgenesis is a disorder of sexual development, characterised by incomplete or defective formation of the ovary or testis due to anomalies of the sex chromosomes or mutations in the genes involved in gonadal development. There is a wide range of phenotypes from normally virilised males, through ambiguous phenotypes, to normal phenotypic females.

- Patients have an increased risk of gonadal tumour formation.
- Dysgenetic gonads show variable degrees of immaturity or dysfunction, which can manifest in a wide range of genital ambiguity. Gonadal dysgenesis can be classified as either complete or partial depending on the gonadal morphology.
- Patients who have a Y chromosome or Y-chromosome material are at increased risk for developing germ cell tumours such as gonadoblastoma. Included in this group are patients with Turner syndrome who have a mosaic karyotype, usually 45,X/46,XY. Prophylactic gonadectomy is often recommended.
- There is often an association with renal abnormalities.
- Gonadal dysgenesis may be asymmetrical - eg, streaked on one side, normal on the other.
- Turner syndrome affects around 1 in 2,500 live-born females. Features include growth failure, gonadal dysgenesis (leading to premature ovarian failure), cardiac anomalies, renal anomalies (including horseshoe kidneys and renal agenesis) and autoimmune disorders. Patients are at increased risk of UTIs and hypertension. Most symptoms of Turner syndrome occur due to the loss of specific genetic material from one of the X chromosomes.

- Swyer's syndrome, 46,XY gonadal dysgenesis, is a rare sex reversal disorder with a female phenotype. The incidence is estimated at 1 in 20,000 to 1 in 80,000 births. Around 30% develop germ cell tumours of the streak ovaries, most commonly gonadoblastoma. Presentation is usually with primary amenorrhoea in adolescence, although there is a morphologically normal (though undersized) uterus.[41]

Disorders of sex development[18]

The formerly called 'intersex disorders' have been changed to 'disorders of sex development' (DSD).[42] [43] This classification has arisen because of advances in knowledge of the molecular genetic causes of abnormal sexual development, controversies inherent to clinical management and ethical issues.

Babies born with ambiguous external genitalia present an immediate problem of sex assignment, which is particularly distressing to parents. Presentation can vary greatly but can include ambiguous genitalia, female genitalia with clitoral hypertrophy, male genitalia with undescended testes, microphallus or hypospadias, and cloacal extrophy. Causes include complete or partial androgen insensitivity, 5-alpha reductase deficiency, congenital adrenal hyperplasia, ovotesticular DSD (formerly true hermaphroditism), and others. Management of intersex conditions is complex and involves making choices regarding a person's assigned gender identity, gender role behaviour, likely sexual orientation, sexual functioning and psychological adjustment.[44]

Findings suggesting the possibility of DSD include:

Apparent male

- Severe hypospadias associated with bifid scrotum.
- Undescended testis/testes with hypospadias.
- Bilateral non-palpable testes in a full-term apparently male infant.

Apparent female

- Clitoral hypertrophy of any degree; non-palpable gonads.
- Vulva with single opening.

Indeterminate

- Ambiguous genitalia.
- Any neonate presenting with ambiguous genitalia is an emergency because 46XX girls with congenital adrenal hypertrophy are at risk of fatal salt loss.

See the separate Ambiguous Genitalia article.

Dr Mary Lowth is an author or the original author of this leaflet.

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