genitalia. These may include bilateral cryptorchidism, perineal hypospadias with bifid scrotum, clitoromegaly, posterior labial fusion, phenotypic female appearance with a palpable gonad, and hypospadias and unilateral nonpalpable gonad. Also included in the DSD category are infants with discordant genitalia and sex chromosomes. Turner syndrome (45, XO) and Klinefelter syndrome (47, XXY) are also DSDs that do not present with ambiguous genitalia.

Pathophysiology

Normal sexual differentiation starts at 7 weeks gestation when fetuses with a Y chromosome begin developing testes. Early on both female (XX) and male (XY) fetuses have a similar reproductive structure. Multiple genes contribute to this process and mutations in these genes can lead to various DSDs. Congenital malformation of the genitalia are most frequently because of androgen deficiency in XY individuals and androgen excess in XX patient; though in many cases no endocrine etiology can be found (Grinspon and Rey, 2014).

Initial evaluation includes karyotype and assessment of adrenal and gonadal function, and this information can be used to categorize the infant into one of three categories:

- Virilized XX (XX DSD)
- Undervirilized XY (XY DSD)
- Mixed sex chromosome pattern

Therapeutic Management

The most common cause of ambiguous genitalia is **congenital adrenal hyperplasia (CAH)**, which can lead to life-threatening salt-wasting adrenal insufficiency in the first weeks of life. Though now a part of neonatal screening in the US, any infant with genital ambiguity should be evaluated urgently. Laboratory testing includes a measurement of 17-hydroxyprogesterone in addition to karyotype with immediate probe for SRY (sex-determining region on the Y chromosome). Serum electrolytes are monitored as signs and symptoms of adrenal insufficiency may include hypoglycemia, hypovolemia, hyponatremia, hyperkalemia, vomiting, and diarrhea. Fluids and electrolytes need to be replaced urgently, and