1 **DISORDERs OF SEXUAL DEVELOPMENT(DSD)**

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2 **What is DSD**

- A condition "In which development of chromosomal, gonadal or anatomical sex is atypical"
- May be diagnosed at birth as ambiguous genitalia: Any case in which the external genitalia do not appear completely male or completely female,or at puberty as primary amenorrhoea or virilization.
- older term as intersex & hermaphrodite are confusing & hurtful

3 **Disorders of sexual development classification**

4 **Sex chromosome disorders**

Turner syndrome

- Result from a complete or partial absence on one X chromosome (45XO)
- It is the most common chromosomal anomaly in females
- Characterised by steak ovaries which consist of fibrous tissue only with no follicles or hormone production

5 **Symptoms**

6 **Clinical features**

- Short stature
- Loss of ovarian function
- Endocrine imbalances(thyroid, diabetes)
- Webbing of the neck,wide carrying angle
- Coarctation of the aorta,inflammatory bowel disease, renal anomalies
- deafness

7 **Diagnosis**

- Usually made at birth from the clinical appearance of the baby or in early childhood due to short stature
- In 10% of cases dx is made at adolescence due to delayed puberty
- The Dx is confirmed by karyotyping

8 **Treatment**

- Growth hormone therapy in childhood
- Estrogen replacement therapy at puberty
- Cardiac surgery (when needed)
- ovum donation & in vitro fertilization (to achieve pregnancy)
- Psychological help
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9 **XY gonadal dysgenesis**

1 • Characterize by non functioning streak gonad ,because of absence of AMH internal female genital tract develop normally
- because of absence of testosterone ,the fetus does not virilize
- Present at adolescence with failure to go into spontaneous puberty
- Management
- Puberty is induced with estrogen
- Dysgenetic gonad has high risk of malignancy & should be removed on Dx
- Pregnancy
- Psychological support

10 **Ovatesticular DSD**

1 • ovarian and testicular tissue exist within the same individual.
- the karyotype is usually of normal female (46XX); in 58% of cases , 13% had 46XX/XY, followed by 46XY (11%).
- commonest combination of ovotestis is for an ovotestis to be on one side and an ovary on the other, with a testis on one side and an ovary on the other being almost as frequent

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1 • Diagnosis of ovotesticular DSD can only be made after gonadal biopsy, and sex of rearing should be determined on the functional capability of the external genitalia after which

inappropriate organs should be removed.

Androgen insensitivity syndrome

- Karyotype of 46XY
- Result from mutations in androgen receptor genes resulting in complete or partial absence of functioning androgen receptors
- The testis is of normal size either in the abdomen or the inguinal ligament
- Due to presence of mullerian inhibitory factor-→inhibit mullerian duct development
- Due to absence of androgen receptor in the wolfian duct,it will regress
- In complete AIS the external genetalia would be of female with blind vagina, in partial form there is different degree of virilization of the external genitalia
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- Usually diagnosed around the time of puberty due to delayed menstruation
- Breast development is usually normal due to conversion of testosterone to estrogen
- There is sparse or absent axillary & pubic hair

Partial androgen insensitivity syndrome at adolescence

Gynecomastia from peripheral aromatase conversion of testosterone to estrogen
Abundant pubic hair implies only partial resistance

Treatment

- There is tendency for testicular neoplasia so it should be removed after pubertal growth complete
- Vaginal dilators or reconstructive surgery
- Psychological counselling

Disorders of androgen synthesis

- 5^{α} reductase deficiency
- deficiency of 5 α - reductase, the enzyme responsible for the conversion of testosterone to dihydrotestosterone,which results in virilization of the external genitalia during embryogenesis. Testosterone is unable to induce virilization during fetal life but at puberty androgen receptors become sensitive to circulating levels of testosterone and therefore a degree of virilization can occur.

- These patients are genetic males who show ambiguous genitalia at birth and at puberty begin to virilize like normal males. This results in penile enlargement, increased facial hair and muscular hypertrophy but breast development does not occur.
- Management of these patients after puberty can be difficult as they themselves may find sexual orientation difficult
- they must be fully assessed before any permanent decisions are made.

46xx DSD

- Congenital adrenal hyperplasia
- autosomal recessive condition
- The clinical picture results from inadequate production of cortisol & aldosterone and the increased production of androgens & steroid metabolites due to adrenal enzyme deficiency, most common is 21-Hydroxylase deficiency which result in elevated levels of androstenedione, 17 - hydroxyprogesterone and testosterone. As this is a disorder is present during fetal life, the elevated levels of androgen lead to virilization of the fetus and therefore clinically female fetuses show clitoral hypertrophy and labioscrotal fusion

Enzyme pathway

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- This condition may be associated with salt losing resulting in hyponatremia & hyperkalemia
- 11-b-Hydroxylase deficiency is less common ,it is characterized by elevation of serum 11-Deoxycortisol and 11-deoxycorticosterone which have strong mineralocorticoid activity resulting in salt retention, hypertension & hypokalemic alkalosis
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- Those individuals with mild deficiencies of the enzyme present in adolescence or adulthood with varying virilizing symptoms & oligomenorrhea and infertility

- A karyotype is essential in the evaluation of the infant with ambiguous genitalia.

- Prenatal diagnosis of adrenal hyperplasia is possible through biochemical and genetic tests
- A pelvic ultrasound: in the infant with ambiguous genitalia to demonstrate the presence or absence of a uterus
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MODES OF TREATMENT

- ❑Steroid replacement :life-long
- ❑Supportive therapy when needed
- ❑Plastic surgery for ambiguous genitalia at early age
- ❑Genetic counseling
- ❑Psychological support

- Mullerian anomalies

46XX Müllerian agenesis

- Mayer – Rokitansky – Küster – Hauser (MRKH) syndrome and here congenital absence of the vagina in a 46XX individual is generally associated with absence of the uterus.
- These patients usually present with primary amenorrhoea with normal secondary sexual characteristics as the ovaries are normally developed

- ultrasound of the abdomen will define the absence of Müllerian structures.
- It must be remembered that a very short vagina may also occur in patients with androgen insensitivity but the assessment of karyotype will differentiate these two groups of patients.
- In all patients found to have MRKH syndrome, the renal tract should be investigated using ultrasound as 40% of patients will have renal anomalies,

Management

- Psychological support
- graduated glass dilators to elongate the vagina
- If failed surgical vaginoplasty
- pregnancy

Transverse vaginal septum/imperforate hymen

- Due to an imperforate membrane at the lower end of the vagina
- Usually recognized at puberty due to retention of menstrual flow gives rise to the clinical features of haematocolpos as cyclical abdominal pain,primary amenorrhoea and occasionally interference with micturition
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- Examination reveals a lower abdominal swelling,. Vulval inspection may reveal the imperforate membrane

Treatment

- If the membrane is thin, then simple excision of the membrane and release of the retained blood resolves the problem.

Diagnostic Evaluation of DSD

- history,
- complete physical examination,
- karyotype
- abdominal/pelvic ultrasonography,
- endocrine studies of adrenal and gonadal steroid secretion
  - 17OHP & androstenedione to excludes CAH due to 21-hydroxylase
  - Electrolytes—should be measured to exclude salt wasting
  - ACTH, cortisol, DHEA, gonadotropins
  - 11-desoxycortisol
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35 **case1**

- Newly born neonate with ambiguous genitalia (labioscrotal fold fusion & clitoromegally), on other phenotypic abnormalities.How would you manage this case?

36 **Case 2**

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- 16 years old girl brought to you by her mother who was anxious because her daughter did not menstruate yet,how would u manage her?
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THANK YOU