Disorders of Sexual Differentiation

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Hermaphroditus
Consensus Statement on Management of Intersex Disorders

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Drop use of “hermaphrodite” and derivatives
Epidemiology

- 1 in 15,000 live births
  - Congenital Adrenal Hyperplasia
  - Mixed Gonadal Dysgenesis
  - Ovotesticular DSD
Genetics, Embryology, and Normal Development
Genetics, Embryology, and Development

- Stepwise development
- Chromosomal gender
- Phenotypic gender
Genetics, Embryology, and Development

- Signaling genes and receptor genes
- *SRY* and *SOX9*
- *WT1* – Testicular agenesis or dysgenesis
  - Denys-Drash Syndrome, WAGR, Frasier Syndrome
- *DAX1*
Genetics, Embryology, and Development

Quigley, Charmian A., Vilain, Eric - Endocrinology, 2148-2190, 2010
Phenotypic differentiation of the external genitalia in female and male embryos, © UpToDate 2014
Evaluation

- Bilaterally non-palpable testes
- Microphallus
- Perineal hypospadias and bifid scrotum
- Clitororomegaly
- Posterior labial fusion
- Palpable gonads in labial folds
- Hypospadias with unilaterally absent gonad
- Discordant phenotype and chromosomal gender
Evaluation - History

- Prenatal androgen exposure
- Maternal virilization
- Family history of amenorrhea
- Family history of unexplained infant deaths
- Homogenous populations or consanguinity
Evaluation

- Karyotype analysis
- 17-OH Progesterone levels
- FISH for SRY
Pathophysiology of DSD
Turner Syndrome

- Stereotypical appearance
- Universally infertile
- Associated with heart defects
47 XXY
Kleinfelter Syndrome

- Physical changes at puberty
- Hypogonadism
- Patients mostly sterile, male
- Many variations based on number of X chromosomes
Congenital Adrenal Hyperplasia
Androgen Excess from CAH
  - 4 types; ± salt wasting, hyperkalemia, hypertension
Normal female gonads
Spectrum of virilized genitalia
Diagnosed by electrolyte abnormalities, deoxycortisol levels

Palpable gonads exclude diagnosis

Maternal dexamethasone early if family history

Cortisol replacement

Most identify as female, have reproductive potential, require feminizing genitoplasty
46 XX
Female Pseudohermaphrodite
46 XX
Female Virilization
Androgen Production Deficit

- Severe enzyme deficiencies often result in death
- Adrenal and gonadal deficiencies
46 XY
Male Pseudohermaphrodite

- Testes sometimes palpable
- Elevated postpartum testosterone
- Gender identity variable
Receptor Deficiency

- Spectrum of genitalia abnormalities
- Complete androgen insensitivity syndrome
  - 1-2% of females with inguinal hernia
- Partial androgen insensitivity syndrome
  - Virilized female, infertile male, undervirilized fertile male

5 α-Reductase Deficiency

- Normal testes – impaired virilization
- Failure of conversion to dihydroxytestosterone
- Patients often raised female

Abnormality of MIS production or receptors

- Normal Wolffian development without regression of Müllerian ducts
- Often normal phenotype with undescended testes, discovered during hernia repair or orchiopexy
Müllerian Inhibiting Substance Deficiency
Leydig Cell Abnormalities

- Hypoplasia, agenesis, or receptor dysfunction
- 46 XY Female phenotype
- Managed similarly to CAIS
Ovotesticular DSD
True Hermaphrodite

- Presence of testes and ovaries
- 46 XX most commonly
- Gonads typically polar
Ovotesticular DSD
True Hermaphrodite
Surgical Therapy in DSD
Surgical Therapy in DSD

- Treatment as varied as presentation
- Considerations
  - Presenting age
  - Concordance of chromosomal and phenotypical gender
  - State of genitalia at presentation
  - Gonadal status
  - Neoplastic potential
Surgical Therapy in DSD

- Surgical Considerations
  - Functional Excretion
  - Cosmesis
  - Sexual Function
  - Reproductive Potential
  - Gender Identity
  - Timing
Psychosocial Considerations

- Essential to have multidisciplinary team
- Best cared for at centers with experience
- Conflicting evidence on age of surgery
Surgical Therapy in DSD

- Long-Term Considerations
  - Psychological follow up
  - Fertility
  - Sexual function and appearance
Feminizing Genitoplasty

- Monsplasty, clitoroplasty, vaginoplasty
- Complete urogenital mobilization
- Vaginal Reconstruction

Feminizing Genitoplasty Outcomes

- Long Term Outcomes
  - Overall favorable, compliance critical
  - Quality of life generally good

Feminizing Genitoplasty
Total Urogential Mobilization

Feminizing Genitoplasty
Monti Tube

Feminizing Genitoplasty
Corporeal Sparing Clitoroplasty

Masculinizing Genitoplasty

- Technically challenging
- Patients typically satisfied with appearance but results variable
  - Penile length
  - Sexual function
  - Urinary symptoms
Masculinizing Genitoplasty

Maria Helena Palma Sircili et al. Long-Term Surgical Outcome of Masculinizing Genitoplasty in Large Cohort of Patients With Disorders of Sex Development. Journal of Urology, The, 2010-09-01, Volume 184, Issue 3, Pages 1122-1127
Psychosocial Considerations

- Debate regarding timing and patient involvement in decision-making
- Family counseling from birth
- Long-term counseling for patients
Transsexualism

- Gender identity, gender dysphoria, gender nonconformity
- Overwhelming urge to be of the opposite gender
- Psychological and biological components
- Gender reassignment
Conclusions
Conclusions

- Significant variation in presentations
- Medical treatment foremost
- Successful management requires multidisciplinary teams
Conclusions

- Surgical options vary and continue to evolve
- Long-term outcomes generally positive
- Timing of operation debatable but most advocate early genitoplasty