Atypical Male Genital Development: Update of Care of Cryptorchidism and Hypospadias

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Cryptorchidism

• Affects 3% of newborn, full term males.\(^1\)
  – Unilateral vs bilateral
  – Palpable vs non-palpable

• 70% of testicles descend in the first 6 months of life

• Approximately 0.8-1% of males have persistent cryptorchidism at one year of life

Cryptorchidism

- “Ectopic”
  - Lie outside the natural path of descent
- “True”
  - Lie within the natural path of descent
- Absent
- Retractile
Causes of cryptorchidism

• Unclear!

• Intra-abdominal phase of descent androgen dependent

• Passage through inguinal canal 28th week combination of mechanical, hormonal, neurotransmitter effects

• Other associated conditions
  – Prune Belly, DSD, genetic disorders
Evaluation of cryptorchidism

- History
  - Descended at birth?
  - Family history
  - Prior inguinal surgery/trauma to area

- Physical examination
  - Frog leg position
  - Lubrication
Evaluation of cryptorchidism

- Need for imaging?
Overall the recommendation is that radiologic evaluation of the non-palpable testicle is not warranted.\textsuperscript{1-3}

Evaluation of cryptorchidism

- Need for imaging?
Evaluation of cryptorchidism

- Hormonal treatment
  - Use of hCG to stimulate testosterone production and produce further descent of the testicle
  - Can also confirm presence of testicular tissue in bilateral, non-palpable testes
Evaluation of cryptorchidism

- **Timing of referral**
  - Immediately if associated with a hypospadias or bilateral non-palpable testes
  - 6 months of age if unilateral with no other abnormalities of genitalia
  - As soon as it is felt that the testicle is not palpable in scrotum in child older than 6 months
Do testicles ascend?

• Reascent of testes after the first year of life can occur in up to 40% of boys

• Most evidenced by higher than expected age at time of orchiopexy

• Ascended testicles
  – Unilateral
  – Identified in childhood
  – Located distal to the inguinal canal

Reasons for orchiopexy

• Prevention of potential sequelae\(^1\)
  – Parental anxiety
  – Testicular cancer
    • Up to 20 fold increased risk of malignancy
  – Subfertility
    • Histologic changes occur in testicles that reside in warmer temperatures
    • Fertility rates with a normal, contralateral testicle are the same as general public (85-90%)
  – Testicular torsion/inguinal hernia
    • Higher torsion rate in undescended testes?

Surgical considerations

• **Timing**
  – 6 months corrected age, or whenever the UDT is identified
  – Post pubertal

• **Approach**
  – Abdominal/laparoscopic
  – Inguinal
  – Scrotal

• **Recovery**
  – Testicular self examinations
Hypospadias: Epidemiology

- Ranges from 0.26 – 4.1 per 1000 births
- Increase incidence in last 3 decades\(^1,2\)
- Environmental and genetic factors (20-25% of cases)
- Racial and ethnic discrepancy:
  - White >> black, higher in Jewish and Italian

Hypospadias risk factors

- Advanced maternal age
- Twin gestation
- Low birth weight
- Endocrine disruption/smoking
- Family history
- Associated syndromes
- Testicular dysgenesis syndrome
  - Hypospadias, cryptorchidism, impaired spermatogenesis and testis cancer
Pathogenesis

- Failure of urethral folds to close properly secondary to disruption of the androgenic stimulation required
  - Also leads to failure of the ventral curvature of the penis to straighten and ventral closure of the foreskin
Hypospadias and IUGR

• Active Malformations Surveillance Program 1972-2012
  – Identified 316/289,365 births
• 52.2% glanular; 11.7% subcoronal, 27.8% penile, 8.2% penoscorpotal
• Highest frequency of IUGR (34.6%) in infants with penoscorpotal hypospadias
• Possible low testosterone and placental HCG during 10-14 weeks gestation

<table>
<thead>
<tr>
<th>Gene</th>
<th>Function</th>
<th>Proposed role in hypospadias</th>
<th>Reference</th>
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<tbody>
<tr>
<td><strong>DKK2, SFRP1</strong></td>
<td>Cell signalling</td>
<td>Wnt inhibitory</td>
<td>Miyagawa et al (2009)</td>
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<tr>
<td><strong>CYR61</strong></td>
<td>Extracellular signalling molecule</td>
<td>Cell proliferation, upregulated in hypospadias</td>
<td>Wang et al (2007)</td>
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<td><strong>GADD45β</strong></td>
<td>Growth arrest</td>
<td>Cell cycle, upregulated in hypospadias</td>
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Rule of 10s

- 10% of fathers
- 10% of siblings
- 10x increased incidence in twins
- 10% have **UDT**
- 10% have **inguinal hernias**
- 10% incidence of **utricle** in those with penoscrotal hypospadias (57% in those with perineal defect)
Spectrum of Hypospadias

50% of cases

- Glanular
- Coronal
- Subcoronal
- Distal penile
- Midshaft
- Proximal penile
- Penoscrotal
- Scrotal
- Perineal
Hypospadias and Epispadias

- Glanular hypospadias
- Penile hypospadias
- Penoscrotal hypospadias (with chordee)
- Scrotal hypospadias (bifid scrotum, chordee)
- Penile epispadia
- Complete epispadia
Presentation

• Incomplete foreskin
• Chordee
• Intersex evaluation: rule of 2/3
  – If 2 of the 3 genital structures are abnormal then evaluate for intersex
  – ie. Hypospadias + impalpable testis
Examples
Chordee (Ventral Curvature without Hypospadias)

Causes

• Skin
• Atretic urethra
• Buck’s or Dartos fascia
• Corpora disproportion

• Normal in fetal phallic development
Principles of Hypospadias Surgery

- Orthoplasty
- Glansplasty
- Urethroplasty
- Scrotoplasty
- Skin coverage

penoscrotal angle
penopubic angle
penoscrotal configuration (i.e. transposition)
multi-layer coverage
To circumcise or not?

- Generally no....

- Megameatus intact prepuce variant
  - If circumcision is started and concern for hypospadias, can complete or abort
Timing of referral

- Surgical repair typically delayed until child is at least 6 months of age

- Parental anxiety

- Immediate referral if concerned for association with other syndromes/DSD
Post-operative Care

- Dressing (tegaderm, coban) x 24 hours
- Urethral stent x 5-10 days
- Antibiotic prophylaxis until stent removed
- Anticholinergic for older children
Complications

Urethrocutaneous fistula
- 5-7% incidence
- More complex repairs: 10-20%
- Repair 6-8 months following initial surgery

Meatal stenosis
- Dilation
- Ventral incision
Complications

**BXO**
Usually presents with meatal stenosis remote from surgery

**Urethral Diverticulum**
Usually secondary to meatal stenosis, large Island flap

**Stricture**
Secondary to ischemia of urethral plate/flap
Current Controversies in Hypospadias/Chordee Repair

• Concerns over genital reconstruction in children before the age of consent / Loss of autonomy of body

• Legislation in 3 states presented that includes a moratorium on surgery in children less than age of majority

• Data exists that supports early surgery for increased risk of complication in operating on older patients
Current Controversies in Hypospadias/Chordee Repair

• Distal or balanitic hypospadias do not always need immediate repair

• Discussion on waiting/observation

• Rates of chordee later in life unknown
• Thank you!