Undescended Testis

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Last Updated:

Tuesday, January 31, 2023

1. Introduction

Undescended testis is one of the most common congenital anomalies in boys, with around 3 in 100 boys born with the condition. Testicular descent occurs throughout gestation, with caudal movement into the scrotum usually noted between 22-27 weeks. However, spontaneous descent may occur postnatally, through the first six months of life. In fact, two thirds of undescended testes will descend spontaneously by age 3 months. In boys with persistent undescended testis, orchiopexy is recommended to bring the testis to the scrotum during the period of 6-18 months of age.

Testicular location may change during childhood, therefore yearly physical examination is recommended to detect any changes in position. Retractile testicles may be manipulated to the scrotum after fatigue of the cremaster muscle (or when the child relaxes) and typically resolves with age and puberty.

Acquired undescended testes, or ascended testes, represent a second cohort in which surgery is recommended by the **AUA Guidelines**.[1] This group may include laterally ectopic testes, entrapped testes after previous inguinal surgery and previously descended testicles that have ascended with longitudinal growth. With vertical growth, the ascended testis will not stay in a dependent position after manipulation into the scrotum on office exam, differentiating this condition from retractile testes. Orchiopexy is recommended for acquired undescended testes after detection.

Undescended testicles are associated with decreased fertility, increased risk of testicular malignancy, risk of torsion as well as increased risk of inguinal hernia. Orchiopexy is recommended to optimize testicular parameters and allow for regular examination.

Keywords

Cryptorchidism, Undescended testicle, Ascended testicle, Orchiopexy, Retractile testicle

2. Diagnosis and Evaluation

Diagnosis of the undescended testis is mainly dependent on the physical examination. As stated in the AUA guidelines, “Providers should not perform ultrasound (US) or other imaging modalities in the evaluation of boys with cryptorchidism prior to referral as these studies rarely assist in decision making (Statement 6, Standard; Evidence Strength: Grade B)” Additional imaging such as CT scans or MRIs do not add additional useful information for the evaluation of most children with UDT. The American Board of Internal Medicine Choosing Wisely Campaign focused on avoidance of ultrasound in boys with cryptorchidism, updated last in 2017.[2]

The physical examination should focus on differentiating a congenital or acquired undescended testis from a retractile testes. Congenital undescended testes are present at neonatal examination, where one or both testicles are not able to be palpated in a dependent scrotal location. An acquired undescended testis presents in childhood, with a previously documented normal scrotal location. It is recommended that testicular exams be performed at each well-child visit to detect any change in examination (AUA Guidelines Statement 2, Standard; Evidence Strength: Grade B).

A retractile testis is one that may be extra scrotal on examination but can be manipulated into a dependent scrotal position, where it remains temporarily after release. Acquired undescended testicles can no longer be manipulated into

the scrotum or immediately re-ascend after being manipulated into more distal location.

Over 70% of undescended testicles should be palpated by an experienced provider. Ectopic testes may be palpated outside of the path of testicular descent such as in a perineal, femoral or penile location, or more commonly in retroscrotal location.

Annual exams are recommended “to monitor for secondary ascent” in boys with retractile testes (AUA Guidelines Statement 9; Standard; Evidence Strength: Grade B). Retractile testes do not appear to benefit from surgery whereas surgery is recommended for congenital and acquired undescended testis. An important cause of acquired undescended testis, or ascended testis, is after a previous inguinal herniorrhaphy which may cause an entrapped testis.

Retractile testes should be followed yearly by the primary care doctor, to ensure ascent does not occur, as this phenomenon has been reported at higher frequency in boys with retractile testes. [3] Once detected, “primary care providers should refer promptly to surgical specialists for timely evaluation (AUA Guideline Statements 3 & 4, Standard; Evidence Strength: Grade B).

Other factors to consider during the initial evaluation:

- Was the baby premature? Per AUA guidelines, “providers should obtain a gestational history at the initial evaluation of patients with suspected cryptorchidism" (Statement 1, Standard; Evidence Strength: Grade B). Surgery is recommended for congenital undescended testis in between the ages of 6 and 18 months of age for babies born at term. For a premature baby, the age should be adjusted to determine when surgery would be appropriate.
- Does the patient have bilateral undescended testes? These patients should be identified in the neonatal period, as disorders of sexual development such as congenital adrenal hyperplasia (46 XX) may present as a virilized male infant with non-palpable testes and phallic structure that may appear normal in size (AUA Guideline Statement 5, Standard; Evidence Strength: Grade A). If severe hypospadias is noted with cryptorchidism, "providers should assess the possibility of a disorder of sex development (DSD)" (AUA Guideline statement 7, Recommendation; Evidence Strength: Grade C).
- Patient potential for fertility and life expectancy: for patients with multiple comorbidities, the risk of surgery may not justify its benefits. The benefit of surgery in broad terms is a reduction in the risk of testicular cancer from around 1% to around 0.3%.[4] Testicular cancer associated with cryptorchidism usually occurs in between the ages of 15 and 35.

Imaging should not be used routinely as noted by AUA guidelines:

“Providers should not perform ultrasound or other imaging modalities in the evaluation of boys with cryptorchidism prior to referral, as these studies rarely assist in decision making… In the hands of an experienced provider, more than 70% of cryptorchid testes are palpable by physical examination and need no imaging. In the remaining 30% of cases with nonpalpable testis, the challenge is to confirm absence or presence of the testis and to identify the location of the viable nonpalpable testis”. “…ultrasound is non-contributory in routine use, with sensitivity and specificity to localize nonpalpable testis at 45% and 78%, respectively”. “The cost and ionizing radiation exposure associated with CT scanning precludes its use. MRI with or without angiography has been more widely used with greater sensitivity and specificity but is deterred by cost, low availability and need for anesthesia. At this time, there is no radiological test that can conclude with 100% accuracy that a testis is absent”. “…regardless of preoperative radiological findings, these studies rarely assist in the decision making and may at times mislead the practitioner due to false positives or false negatives in determining the presence of a testicle.”

3. Prevalence

For congenital undescended testis, the prevalence at birth is around 3% but that decreases to around 1% by age 3 months. The prevalence is much higher for premature babies, depending on gestational age and weight, and was reported to be as high as 30-45%.

Acquired undescended testes, or ascended testes, appear to be just as prevalent as congenital undescended testis. Age

distribution for orchiopexy is biphasic with one peak corresponding to congenital UDT early in life and a second one corresponding to acquired UDT in late childhood. Ascended testes peak around 8 years of age, and prevalence is estimated at 1%-7%. [5,6]

4. Risk Factors and Pathophysiology

4.1 Risk Factors:

Some families exhibit a genetic predisposition for this condition but as in many other urologic conditions, most cases appear to occur de novo. Known risk factors include prematurity and low birth weight (independent of gestational age), as well as association with many named genetic syndromes.

Maternal alcohol consumption has been inconsistently associated with cryptorchidism.[7] Prenatal cigarette smoking exposure is associated with increased risk of cryptorchidism.[8] Exposure to paracetamol during the period in pregnancy when male sexual differentiation takes place, increases the risk of cryptorchidism.[9] Congenital Zika syndrome has been associated with increased risk of cryptorchidism in a small series (34%) of boys with microcephaly.[10]

4.2 Testicular Descent and Anatomic findings:

Testicular descent is regulated by many factors and depends on intact hypothalamic-pituitary-gonadal axis. As such, conditions of disrupted hormonal regulation are associated with increased incidence of cryptorchidism. Androgens and related genes such as Insulin-like 3 (INSL3), Relaxin/Insulin-like family peptide receptor 2 (RXFP2) have been implicated in testicular descent, particularly the fetal gubernaculum-cremaster muscle complex. Insulin 3 mainly regulates the intraabdominal phase (from kidney to groin) and testosterone is primarily responsible for the inguinoscrotal phase as well as the gubernaculum. The gubernaculum enlarges at some point before the testis is pulled into the scrotum and so it seems to play an important role in testicular descent. Despite the elucidation of these regulatory genes, reliable detection of genetic anomalies has been unsuccessful for most boys with cryptorchidism, as the underlying pathophysiology is likely heterogenous and polygenic.

Undescended testes are associated with structural anomalies such as abnormal epididymal morphology, germ cell depletion, and risk of germ cell tumors.[11] Orchiopexy is reported to reduce risk of germ cell tumors and may allow catch up growth of the affected testis.[12]

4.3 Ascended or Acquired Undescended testis:

Ascended testicles may occur during childhood and may be initially diagnosed as retractile testes. With growth, they may move to a suprascrotal location, and be unable to be brought to dependent scrotum. Yearly well-child examinations are recommended to confirm testicular position and allow for prompt referral of children with concerning exams. Referral delay in patients with cryptorchidism has been associated with history of normal newborn scrotal exam, and new provider performing yearly examination, indicating likely ascended testes in these cases.[13] Proximal hypospadias and has been linked to increased risk of testicular ascent, possibly highlighting role of androgen signaling.[14] In boys with retractile testes, position may change over time, indicating ascent.[15] Reports have linked neuromuscular conditions such as cerebral palsy to increased risk of ascended testis over time, highlighting need for yearly examinations in all children.[16]

5. Epidemiology

Maternal Factors: Maternal alcohol consumption has been inconsistently associated with cryptorchidism.[7] Prenatal cigarette smoking exposure is associated with increased risk of cryptorchidism.[8] Exposure to paracetamol during the period in pregnancy when male sexual differentiation takes place, increases the risk of cryptorchidism.[9] The newly described congenital Zika syndrome has been associated with increased risk of cryptorchidism in a small series (34%) of boys with microcephaly.[10]

5.1 Future implications:

Fertility: Unilateral cryptorchidism rarely has an impact on fertility parameters. Attempts to link histology and germ cell

characteristics at time of orchiopexy to future parameters such as sperm density and hormonal profiles have been largely unreliable. [17] Men with a history of bilateral cryptorchidism have reduced paternity rates of approximately 65% which is significantly lower than the general population. [18]

Malignancy Risk: Orchiopexy appears to reduce risk of testis cancer, more significantly if performed prior to puberty. Relative risk of testis cancer is reported to be 2-2.4 when surgery is done before puberty compared to a relative risk of 5-6.2 after puberty. The risk of malignancy does not appear to be different among different prepubertal ages.

With regards to the above two points, a population-cohort study of 350,000 Australian children, assessed the rates of testicular cancer, paternity, and use of assisted reproductive technologies[19]. The study showed statistically significant increased risk of testicular cancer and infertility, as well as decreased paternity in patients that were operated for a unilateral undescended testis compared to controls. However, a close look at the numbers reveals that although statistically significant, the risks are so low to not warrant excessive focus on them during parental counseling:

- 7,499 patients with unilateral UDT
    - 27 had testicular cancer (0.36%)
    - 127 used Assisted reproductive technologies (1.7%)
    - 2,016 fathered children (27%)
- 341,000 controls
    - 476 had testicular cancer (0.14%)
    - 2,529 used ART (0.7%)
    - 107,006 fathered children (31%)

Table 1

	UDT	Control
Testicular cancer	0.36%	0.14%
ART	1.7%	0.7%
Fathered children	27%	31%

[4]Future risks should be conveyed to the family and patient, including risk of infertility and cancer risk, as recommended by the AUA guidelines (Statement 16, Clinical Principle), keeping in perspective the very low risks as a percentage or in absolute numbers.

Risk of testicular torsion: some previous studies[20] reporting an association in between UDT and torsion had made the diagnosis of UDT at the time of presentation for testicular torsion, raising the validity of the diagnosis of UDT – given the fact that torsed testicles do retract into the groin. In contrast, a new study[21] identified 11 boys who were scheduled for orchiopexies which, while waiting for surgery, developed testicular torsion. These 11 cases corresponded to 10% of testicular torsion cases seen in between 2013 and 2018 at the authors institution. Median age was 9 months (range 1-22 months). Salvage rate was low at 18%. Clinically, 4/11 cases were thought to have an incarcerated hernia preoperatively. Over the same period, the authors performed 1440 orchiopexies, which translates to an incidence of torsion of 0.7% or 1/130 cases – much higher than the incidence of torsion of1/5000 in the general population.

5.2 Patient Evaluation:

Physical examination is the mainstay of preoperative evaluation. Patients may be examined in various positions including supine, frog leg and squatting. In difficult examinations, lubricating jelly, soap or hand sanitizer may aid in palpation of the groin, as the testis may “slip” under the lubrication. It is critical to fatigue the cremaster muscle to distinguish between retractile and truly undescended or ascended testes. Over 70% of undescended testicles should be palpated by an experienced provider. Ectopic testes may be palpated outside of the path of testicular descent such as in a perineal, femoral or penile location, or more commonly in retroscrotal location.

5.3 Investigations:

Imaging studies are not recommended in the evaluation of patients with undescended testes.

6. Medical Treatment

According to the AUA Guideline Statement: “Providers should not use hormonal therapy to induce testicular descent as evidence shows low response rates and lack of evidence for long-term efficacy. (Standard; Evidence Strength: Grade B)”. For this reason, medical therapy is generally not practiced in the United states. However, there is some indirect evidence suggesting that adjuvant hormonal therapy could improve fertility when combined with orchiopexy, [22] but the cohort of patients who would benefit from such an approach has not been defined. European guidelines do recommend endocrine treatment with GnRH analogues for boys with bilateral undescended testis to preserve their fertility potential.[23]

7. Surgical Management

Orchiopexy is recommended for testes which are not in a dependent intrascrotal location, with goal of bringing the testis to the scrotum. Additional surgical goals include treatment of a patent processus vaginalis or inguinal hernia, reduction of risk of testicular torsion, and reduction of traumatic risk of inguinal testis. The posterior approach to dissecting the hernia sac appears to facilitate the dissection and the teaching of the procedure (see **http://meeting.neaua.org/abstracts/2014/39.cgi**). All orchiopexies carry the risk of injury to testis and vas deferens, with subsequent atrophy. Inadequate position of the testis requiring additional intervention may also rarely occur.

Timing of surgery depends on initial presentation, but for congenital undescended testis, it is recommended to perform an orchiopexy for congenital UDT in between 6-18 months of age (corrected for gestational age), per AUA guidelines (Guideline statement 11, Standard; Evidence Strength: Grade B). If the testis is palpable, inguinal or scrotal orchiopexy may be performed depending on surgeon preference and testis location. Adherence to sound surgical principles is critical to protect cord structures including the gonadal vessels and vas deferens, repair the patent processus vaginalis if present, and safely transition the testis to a sub-dartos pouch within the scrotum. Preoperative care involves standard surgical preparation, and counseling regarding risk of infection, bleeding, testicular injury, atrophy, injury to vas deferens, ascent of testis postoperatively and/or presence of hernia which may require repair. Patients and families are counseled on the need for serial exams to ensure proper testicular position and character after orchiopexy.

Several maneuvers are employed to allow the testis to reach a dependent position on the scrotum without any tension. Although division of the cremasteric fibers is thought to prevent reascend of the testis, Bianchi et al did not find that it provided with any extra length. On the other hand, they found that division of the processesus vaginalis provided a

further 1.5-3.5 cm of descent in their series of 120 transcrotal orchidopexies. Also, they realized that retroperitoneal vessel mobilisation through an additional groin incision provided a further 1-1.5 cm of testicular descent in the 5 patients where that was needed.[24]

Once adequate length is achieved for the testis to be positioned in the scrotum, a number of techniques may be used to secure it in place. The most common variation in technique is whether to use a fixation suture through the tunica albuginea of the testis, or “transparenchymal fixation”. With this method, the testis is secured via either an absorbable or non-absorbable suture, single or multiple, taken through the tunica albuginea of the testis to the surrounding dartos.[25] This commonly used technique has provided the historically high success rates established by many large orchiopexy studies to date.[26,27] The necessity of transparenchymal fixation has however been questioned over recent decades. Several studies showed that scarification achieved with parietal tunica vaginalis eversion alone produced excellent fixation similar to tunica vaginalis eversion with non-absorbable or absorbable sutures.[28,29] Moreover, some critics of transparenchymal fixation have reported an association with adverse spermatogenesis, unfavorable histopathologic changes of the parenchyma, and increased tissue inflammation, with many of these demonstrated in animal models.[30,31] Broad conclusions regarding the isolated impact of suture fixation across the tunica albuginea for undescended testis have not been determined, but in light of these findings, the non- tunical orchiopexy has become another commonly used technique.[32] In the non-tunical orchiopexy, the testis is positioned into a scrotal subdartos pouch and absorbable sutures placed only at the circumference of the pouch opening through the visceral layer of the tunica vaginalis. High success rates similar to transparenchymal fixation rates have been reported.[33] The European Association of Urology Guidelines advises the non-tunical orchiopexy, whereas the American Urological Association does not explicitly advise one fixation technique over the other.

For testes which are non-palpable even under anesthesia, diagnostic laparoscopy is recommended, to inspect for intraabdominal testis. Alternatively, the scrotum could be explored first looking for a testicular nubbin or a normal testis, potentially obviating the need for laparoscopy in the majority of cases.[34] When a nubbin is found during scrotal exploration, it should be sent for pathological confirmation to avoid missing an intraabdominal testis when only scrotal exploration is performed, or in cases where laparoscopy did not reveal a testis. In the past, the removal of a testicular nubbin was recommended when blind end vessels reached a closed ring, due to the fact that a small percentage of nubbins had germ cells. However, the risk of cancer in a nubbin is likely to be close to zero[35] and thus a scrotal exploration to remove a nubbin might not be warranted in these cases.

If a testis is found during exploratory laparoscopy, surgical options include laparoscopic orchiopexy without division of the gonadal vessels (single stage) or Fowler Stephens (FS) Orchiopexy (single or two stage approach).

- **Laparoscopic orchiopexy without division of gonadal vessels**: For a standard laparoscopic orchiopexy, the testis is dissected off a triangular pedicle containing the gonadal vessels and the vas. The testis is brought down medial to the epigastric vessels (Prentiss Maneuver).
- **One stage FS orchiopexy**: In the laparoscopic one stage Fowler Stevens orchiopexy, the gonadal vessels are divided, and the testis is dissected off a pedicle of the vas and brought down in one stage.
- **Two stage FS orchiopexy**: In the two stage Fowler Stephen’s laparoscopic orchiopexy, the vessels are divided with clips at the first stage. After six months, the testis is mobilized and brought down in a second stage, to allow collateral blood flow through the deferential artery.

In 1959 Fowler and Stephens initially recommended ligation of the spermatic vessels as far from the testis as possible.[36] Then in 1996, Koff et al suggested that ligating as close to the testis as possible might be better. Laparoscopic orchiopexy has risks inherent to both orchiopexy and laparoscopic procedures including risk of bowel injury, herniation, testicular injury/atrophy, indirect hernia as well as risk of bladder injury during dissection of the new canal for spermatic cord during placement into scrotum.

If no testis is found during exploratory laparoscopy one must determine the presence of either blind ending vessels or a testicular nubbin to completely rule out missing a testis The vas deferens has different embryology from the testicle and can be dissociated from the testis, and thus is not a good guide to find the testis.

- If the internal ring is closed but vessels are going into it, a scrotal exploration usually will find a testicular nubbin.
- If vessels are going into an open inguinal ring, one can usually push the testis into the abdomen but if not inguinal or scrotal exploration would be warranted.

In cases of acquired or entrapped UDT it is recommended to perform an orchiopexy soon after the diagnosis. Often the ascended testis may be approached via scrotal approach depending on position of testis. In this population, 20% will have a patent processus vaginalis, which can be repaired through a single incision, or a standard inguinal incision.[37]

The postpubertal boy with an undescended testis represents a challenge. These patients are at an increased risk of testicular cancer and should be counseled regarding risks of orchiopexy. Orchiectomy is an option if the patient has a contralateral normal testis.

Postoperative care of the patient after orchiopexy includes use of multimodal pain control. We employ intraoperative regional anesthesia, or local blocks, nonsteroidal anti-inflammatory medications such as ibuprofen, and acetaminophen for initial pain control Opiods are used sparingly for refractory pain, however many patients have excellent pain control without need for such medication prescriptions.

8. Important references

1. Age at surgery for undescended testis and risk of testicular cancer[4]

Seminal paper that demonstrated that the risk of testicular cancer is around 2-3 times if the orchiopexy is performed before puberty and around 5-6 times if it's done after puberty compared to the general population. Although early orchiopexy could confer benefits with regards to fertility potential, early orchiopexy does not seem to confer benefits with regards of reduction of testicular cancer as long as the orchiopexy is performed before puberty. This information is important when counseling families regarding timing of orchiopexy.

2. The epidemiology of congenital cryptorchidism, testicular ascent and orchiopexy[11]

This paper reviews risk of acquired cryptorchidism and reports spontaneous ascent of testis over time, from scrotal location. It highlights the need for continued examination of testes throughout childhood, to diagnose testicular ascent. It additionally reports increased risk of ascent in boys with retractile testes, emphasizing need for repeat examinations over time to ensure testis is in an appropriate position prior to puberty.

3. Cryptorchidism and Fertility[18]

This paper integrates more recent evidence pertaining to fertility and orchiopexy. The paper highlights early orchiopexy has more favorable outcomes in terms of germ cell and spermatogenesis. It additionally notes more severe outcomes in terms of delayed orchiopexy or bilateral cases and adds pertinent information for counseling patients and families in these complex cases.

4. Scrotal exploration for unilateral nonpalpable testis[34]

Traditionally, the non- palpable testis has been approached by laparoscopy first, with scrotal or inguinal exploration as needed if either blind vessels are found or an open inguinal ring suggests an inguinal testis. In this study, Snodgrass et al demonstrated that performing a scrotal exploration first, avoids laparoscopy in the majority of patients. The only downside of exploring the scrotum first would be ending up doing a 2 stage Fowler Stephens orchiopexy, in which case the scrotal incision would have been unnecessary. Scrotum exploration first works best for surgeons that prefer one stage laparoscopic orchiopexies with or without preservation of the testicular vessels as in this situation the scrotal incision would always be used. Also, scrotal exploration works best for surgeons used to doing their orchiopexies with the scrotal approach as they are more accustomed to exposing the entire area in question through the scrotum.

5. Puberty stage and spontaneous descent of acquired undescended testis: implications for therapy?[38] Further evidence for spontaneous descent of acquired undescended testes.[39]

These two studies are interesting as they managed boys with ascending testis without surgery until puberty, at which time they observed a high incidence of spontaneous re-descent. The current AUA guidelines recommended orchiopexy for

acquired undescended testis soon after diagnoses which is not what was done on these two studies. These studies can be kept in mind when surgery would not be ideal (comorbidities) in cases of acquired UDT.

6. AUA Guideline: Cryptorchidism[1]:

This guideline reviews current literature and makes recommendations about management of undescended testes both congenital and acquired as well as treatment options.

Videos

Inguinal Orchiopexy for Undescended Testis

Laparoscopic orchiopexy

Scrotal orchiopexy

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