A nine-year-old Hispanic boy presents for evaluation of bilaterally nonpalpable testes (Figure 1). Exploratory surgery performed in Mexico when he was 18 months of age failed to identify either testicle. An endocrinology assessment that includes human chorionic gonadotropin (hCG) stimulation testing is done at Indiana University Health. Values for serum testosterone, luteinizing hormone, follicle stimulation hormone, and Müllerian inhibiting substance are all within age-appropriate normal limits.

Figure 1. Photograph of external genitalia revealing an empty scrotum

What is IU Health Physicians?
IU Health Physicians brings together Indiana University School of Medicine faculty physicians, IU Health-affiliated physicians and private practice physicians to form the fastest-growing, most complete, multi-specialty practice group in Indiana. This unique partnership gives our highly skilled doctors access to innovative treatments using the latest research and technology.

Our goal is to provide seamless patient care through an integrated and coordinated delivery health system. It will also improve access for patients and referring physicians, provide an excellent environment for world-class scientific research, and further our academic commitment to tomorrow’s health-care professionals.
Cryptorchidism, the incomplete descent of the testicle into the dependent scrotum, is the most common genitourinary disorder of childhood, occurring in approximately 30 percent of premature male infants and between three and five percent of full-term baby boys. Unilateral cryptorchidism is more than twice as common as bilateral cryptorchidism, and the right side is more likely to be affected than the left.

“Cryptorchidism is a manifestation of abnormal migration of the testes during the third trimester,” says Martin Kaefer, MD, professor of urology at the Indiana University School of Medicine. “Alternatively, the testicle can take an anomalous course and end up in an ectopic location (Figure 3). This presentation is unusual, however, accounting for fewer than one percent of all cases of cryptorchidism.”

Testicular descent continues in many patients throughout the first year of life, at which time the incidence of cryptorchidism is about 0.8 percent. Nonetheless, most testes that descend spontaneously do so within six months after birth, driven largely by the testosterone surge that occurs during that period.

When both testes cannot be palpated, hCG stimulation testing is performed to trigger testes production by Leydig cells. Rising serum testosterone levels indicate the presence of testicular tissue. Conversely, a negative hCG stimulation test virtually establishes the diagnosis of anorchism.

Epidemiology

The majority of children with an undescended testis have no associated medical problems. Conditions that are linked to a higher incidence of cryptorchidism include prematurity and low birth-weight, congenital disorders of testosterone secretion or action, abdominal wall and neural tube defects, and cerebral palsy. Cryptorchidism is also a characteristic of various genetic syndromes, such as trisomy 13 and 18 and Prader-Willi syndrome, and risk is approximately three-fold higher in families with a previously affected relative.

Pathogenesis

Normal testicular descent proceeds in two phases. Transabdominal migration, phase one, occurs at seven to 15 weeks of fetal development and entails enlargement of the genitoinguinal ligament (gubernaculum) and regression of the cranial suspensory ligament. Phase two involves transinguinal migration of the gubernaculum and testes from the lower abdomen to the scrotum. This phase begins at seven months gestation and is usually completed by the end of the third trimester.

The exact molecular mechanisms responsible for normal testicular descent are incompletely understood, and even less is known about the pathogenesis of cryptorchidism.

“Most evidence supports a central role for local testosterone in the transinguinal phase of testicular descent,” Dr. Kaefer says. Nevertheless, most individuals with an undescended testis have normal testosterone levels. Recent evidence suggests that there may be mutations in genes responsible for proper body segmentation and testicular positioning (e.g., homeobox genes). “There is data to suggest that the incidence of cryptorchidism is rising,” notes Dr. Kaefer. “Increasing exposure to environmental compounds that can influence hormonal balance—that is, act as an estrogen or as an androgen antagonist—may explain this increase. Both animal and human epidemiologic data support a relationship between undescended testicle and various chemicals, including dichlorodiphenyltrichloroethane (DDT); certain plastic additives, such as phthalates; and naturally-occurring phytoestogens common in soy products.”

A genitourinary evaluation reveals a normal young male of Tanner stage I prepubertal physical development (Table 1). The penis is normal in size with the urethral meatus on the glans. No testes are palpable in the scrotum or groin.

### Table 1. Tanner Stages of Physical Development in Males

<table>
<thead>
<tr>
<th>Stage</th>
<th>Physical Characteristics and Age</th>
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<td>Tanner I</td>
<td></td>
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• No pubic hair (prepubertal)  
• Testicular volume <1.5 mL  
• Penis ≤3 cm  
• Age: ≥9-10 years |
| Tanner II |  
• Small amount of long, downy hair with slight pigmentation at the base of the penis and scrotum  
• Testicular volume 1.6-6 mL  
• Skin on scrotum thins, reddens, and enlarges  
• Penis length unchanged  
• Age 10-11.5 years |
| Tanner III |  
• Hair becomes coarse and curly and begins to extend laterally  
• Testicular volume 6-12 mL  
• Scrotum further enlarges  
• Penis lengthens to ~6 cm  
• Age 11-13 years |
| Tanner IV |  
• Adult-like hair quality extending across pubis but sparing medial thighs  
• Testicular volume 12-20 mL  
• Scrotum further enlarges and darkens  
• Penis increases in length to 10 cm  
• Age 12.5-15 years |
| Tanner V |  
• Hair extends to medial surface of thighs  
• Testicular volume >20 mL  
• Adult scrotum  
• Adult penis of 15 cm  
• Age 14-15+ years |
Diagnosis

The first step in the preliminary evaluation of undescended testicle is a thorough history (Table 2) and physical examination, generally performed by the pediatrician or family practitioner. Imaging in this setting is usually unnecessary and of minimal benefit, for while ultrasound, CT, and MRI are very good at identifying the presence of a testicle outside the scrotum, none can provide 100 percent confirmation that a testicle is absent. Because malignancy is a possible consequence of undescended testicle, complete assurance of the presence or absence of a testicle is critical to clinical decision-making.

“...a general system-based physical examination is carried out in a warm, child-friendly room, with the patient placed on the table in a frog-leg position,” describes Dr. Kaefer. “A common mistake is to initially touch the scrotum since this frequently elicits a strong cremasteric reflex (Figure 4a). Instead, the examiner should put one hand on the child’s abdomen just above the groin before touching the inner thigh or scrotum. This approach can be extremely helpful in blocking the testis from retracting into the high groin or abdomen when the cremasteric reflex is elicited (Figure 4b).

Next, the physician places the index and third finger under the scrotum and feels for the testicle with the thumb,” Dr. Kaefer continues. “If it cannot be felt, gentle palpation over the inguinal canal may be successful in locating the testicle.” An ectopic testicle should be sought outside the inguinal canal, and the contralateral testis should be evaluated. Contralateral hyper trophy may be seen in patients with a nonpalpable testicle, and when the enlarged testis is 1.8 cm or greater, it predicts monorchia (e.g., unilateral absence of the testicle) with an accuracy of about 90 percent.6

“...if a retractile testis can be manipulated into the scrotum and remains in place, no treatment is necessary,” says Dr. Kaefer. “If the testicle can be felt but not repositioned downward, it is a true inguinal undescended testicle. Approximately 90 percent of undescended testes are associated with a patent processus vaginalis,7 and treatment consists of hernia repair at the time of orchidopexy. When the examiner is unable to detect the presence of a testicle in the groin, the testicle may be located in the abdomen or be absent. This situation always requires further evaluation.”

Timing of Referrals

Because of the possibility for spontaneous testicular descent during the first six months of life, infants with cryptorchidism generally do not require an immediate consultation with a pediatric urologist with two notable exceptions: 1) children with cryptorchidism and hypospadias and 2) those with bilateral nonpalpable testes.

“The combined findings of cryptorchidism and hypospadias often suggest the existence of a disorder of sexual differentiation,” Dr. Kaefer reports. “Published data suggest that up to 30 percent of children with a combination of these two findings have a genetic or anatomic finding that is not in complete agreement with male gender.7 Additionally, the finding of bilateral nonpalpable testes in the absence of other external genital anomalies may on rare occasions indicate a life-threatening condition in the neonatal period (i.e., salt-wasting endocrinopathy). The differential diagnosis includes anorchism, undescended testes, and congenital adrenal hyperplasia with extreme masculinization.”

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Diagnostic laparoscopy is performed and visualizes normal-appearing bilateral testicles approximately 3 cm above the internal inguinal ring (Figure 5c). Laparoscopy is terminated.

Laparoscopy is the most accurate modality for locating a non palpable testis. Abdominal access is achieved by inserting a port through an infraumbilical site.

The child undergoes abdominal exploration, and an atraumatic clamp is placed on the main testicular vessels bilaterally. A Doppler pulse is present within the testicle. The right testicle is left in place for blood flow traveling with the vas deferens to perfuse the testicle. The left one-stage Fowler-Stephens orchidopexy is performed, allowing blood flow traveling with the vasa deferens to perfuse the testicle. The right testicle is left in place for microvascular autotransplantation to be performed in six months.
In the hands of skilled surgeons, overall success rates for MTA range from 87 to 95 percent. Because of the technical difficulty of the surgery and the extended recovery period, however, it is primarily reserved for patients with bilateral undescended testes.

**References**


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Dr. Kaefer received his medical degree from Northwestern University Medical School in Chicago, IL, did his residency training in urology at the IU School of Medicine, and completed a fellowship in pediatric urology at Harvard Medical School in Boston, MA. His clinical and research interests include the management of fetal urinary tract obstruction, urinary incontinence, pediatric renal stones, and genital anomalies and undescended testicles.

Dr. Kaefer is certified by the American Board of Urology and is a member of several professional organizations. The author of nearly 100 journal articles and textbook chapters, Dr. Kaefer lectures extensively in the United States and abroad.

For the last decade, Dr. Kaefer has led an annual medical mission trip to Central America, where he and a team of pediatric urologists from across the United States have operated on more than 500 patients with complex urological problems.

**At the time of microvascular testicular autotransplantation (MTA), surgeons determine that the inferior epigastric artery is not of adequate luminal diameter. Microvascular transfer is accomplished using the deep circumflex iliac artery and the inferior epigastric vein. Follow-up at 10 months shows both testicles are positioned within the scrotum, and a strong Doppler pulse is present bilaterally.**

**Figure 5. Bilateral undescended testes**

“Microvascular testicular autotransplantation is a challenging procedure that requires both a highly trained microvascular surgeon and pediatric urologist,” says Dr. Kaefer. “The inferior epigastric vessels are generally used; when they are not suitable, innovative surgical techniques, such as those used in the 10-hour procedure, patients must be immobilized for five to seven days.”

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Fowler-Stephens orchidopexy may be performed in one or two stages and involves transsecting the main testicular blood supply in anticipation that the gonad will survive mobilization using the collateral blood supply provided by the vasa efferentia that travels with the vas deferens. Success rates range from 96 to 99 percent for standard procedures in which all blood supply to the testicles is preserved. When the testicles are positioned very high in the abdomen, Dr. Kaefer and his colleagues generally begin by performing MTA on one side only. Following successful MTA, the surgeons and parents discuss the next step: repeating the procedure on the other side; performing a Fowler-Stephens orchidopexy; or, in rare cases, removing the contralateral testicle. Leaving a nonpalpable testis in place is not an option because of the risk, albeit small, of cancer.

“In cases where one testicle is absent at birth or its high location precludes successful orchidopexy, parents are reassured that the probability of their boy fathering a child is quite high,” Dr. Kaefer concludes. “Research has shown that there are only marginal differences in fertility between men with one versus two testes. In both populations, the probability of conception approaches 90 percent at one year, provided that certain detrimental behaviors (i.e., smoking, drug use) are not practiced, and there are no female-based fertility concerns.”

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