The Undescended Testis

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the child with cryptorchidism or an “empty scrotum” represents one of the most common problems referred to the pediatric urologist or surgeon. The disorder occurs in approximately 0.08% to 1.0% of male children, although the incidence may be increasing. Despite this relatively high rate of occurrence, very little is known about the etiology of the disorder. Surgery continues to be the cornerstone of therapy for the correction of cryptorchidism.

The purpose of this review is to acquaint the reader with a basic understanding of the pathogenesis, pathophysiology, and complications associated with the undescended testes and to discuss the treatment methods used at our institution.

EPIDEMIOLOGY

The incidence of testicular maldescent is directly related to the maturity and the birth weight of the infant (Table 1). In the full-term male with a birth weight ≥ 2,500 g, the incidence of cryptorchidism is between 3% and 4%, while in the premature it approaches 30%. As the weight of these infants approaches 2,500 g, the majority of previously undescended testes have reached the scrotum spontaneously. By 1 year of age, virtually all testes that might be expected to descend spontaneously will have done so.

Recent data have suggested that the incidence of cryptorchidism may have doubled over the past 20 years, but this may be simply due to either greater awareness of cryptorchidism by the practicing physician or to diagnostic confusion with a more common anomaly, the retractile testis. In 10% of patients with cryptorchidism, the anomaly is bilateral. Unilateral or bilateral anorchism is found in approximately 4% of patients with cryptorchidism.

EMBRYOLOGY AND MECHANISM OF TESTICULAR DESCENT

In the human, by the sixth week of gestation the primordial germ cells have made their way from the yolk sac to the genital ridges. The gubernaculum appears at this time as a ridge of mesenchyme extending from the genital ridge to the site of the future scrotum, the genital swellings. The indifferent gonad begins its differentiation into the testis during the seventh week of gestation, and müllerian inhibiting factor (MIF) and testosterone (T) are secreted by the fetal testis during the eighth week of gestation. MIF, secreted by the Sertoli’s cells, induces regression of the müllerian ducts, whereas T, secreted by the fetal Leydig’s cells under maternal human chorionic gonadotropin hormone regulation (HCG), induces development of the epididymis and vas deferens (wolfian duct structures). From the ninth to the 15th weeks, the external genitalia develop; at this time the fetal testis lies in an intraabdominal position, proximal to the internal inguinal ring.

Between the 12th week and seventh month of gestation, a peritoneal out-pouching, the processus vaginalis, reaches the scrotum. At the seventh month continued on page 42
**Brief Summary of Prescribing Information**

**DESCRIPTION**
Erythromycin is produced by a strain of Streptomyces erythreus and belongs to the macrolide group of antibiotics. It is basic and readily forms salts with acids. The base, the lactate, and the sodium are poorly soluble in water. Erythromycin is available as an oral suspension suitable for oral administration.

Erythromycin PO and Ery-Drops erythromycin ethylsuccinate for oral suspension when reconstituted with water, forms a suspension containing erythromycin ethylsuccinate that ranges between 100 and 500 mg per 5 mL (tetrasodium phosphate buffer 0.1 M, pH 3.1, per 0.5 mL [diluted] with an equal volume of water). Erythromycin PO (500 mg reconstituted with water) forms a suspension containing erythromycin ethylsuccinate equivalent to 400 mg of erythromycin per 5 mL (tassium phosphate 0.1 M, pH 4.0) with an appearance similar to that of a buffered banana flavor. After mixing, ERY should be stored below 77°F (25°C) and used within 30 days; refrigeration is not required. These products are intended primarily for pediatric use but can be used in adults.

**INDICATIONS**

**Pediatric**

Erythromycin PO and Ery-Drops Caramel, polyoxyethylene, sodium citrate, sorbic acid, xanthan gum, artificial flavors and other ingredients.

**CONTRAINDICATIONS**

Erythromycin is contraindicated in patients with known hypersensitivity to this antibiotic.

**PRECAUTIONS**

Erythromycin is principally excreted by the liver. Caution should be exercised in administering the antibiotic to patients with impaired hepatic function. There have been reports of hepatic dysfunction, with or without jaundice, in patients receiving oral or intravenous products.

**ADVERSE REACTIONS**

The most frequent side effects of erythromycin preparations are gastrointestinal, such as abdominal cramping and discomfort, and are dose related. Nausea, vomiting, and diarrhea occur infrequently with usual oral doses. During prolonged or repetitive therapy, there is a possibility of overgrowth of nonsusceptible bacteria or fungi. If such infections occur, the drug should be discontinued and appropriate therapy instituted.

**HOW SUPPLIED**

Erythromycin PO (erythromycin ethylsuccinate for oral suspension, USP) is supplied in bottles of 100 mL NDC 0074-6302-12, 250 mL NDC 0074-6303-11, and 500 mL (ABNOPC) package NDC 0074-6302-00. Each 5 m (diluted) of reconstituted suspension contains activity equivalent to 200 mg erythromycin.

Erythromycin PO (erythromycin ethylsuccinate for oral suspension, USP) is supplied in bottles of 60 mL NDC 0074-6005-40, 100 mL NDC 0074-6303-13, 250 mL NDC 0074-6305-53, and 500 mL (ABNOPC) package NDC 0074-6304-18. Each 5 m of reconstituted suspension contains activity equivalent to 400 mg of erythromycin.

Ery-Drops (erythromycin ethylsuccinate for oral suspension) is supplied in a 100 mL NDC 0074-6302-50. Each 5 m of reconstituted suspension contains activity equivalent to 100 mg of erythromycin.

After reconstitution, Ery-Max should be stored below 77°F (25°C) and used within 30 days; refrigeration is not required.

**REFERENCE**


**Dosage Guidelines for Erythromycin**

**Pediatric**

In mild to moderate infections the usual dosage of Erythromycin for children is 15-25 mg/kg/day in equally divided doses.

**Classification**

The antibiotic classification is based, in part, on whether the drug penetrates to the inner in guinal ring.
TABLE 2

<table>
<thead>
<tr>
<th>Organ</th>
<th>Hormone</th>
<th>Disorder</th>
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<tbody>
<tr>
<td>Hypothalamus</td>
<td>GnRH</td>
<td>Kallmann's syndrome</td>
</tr>
<tr>
<td>Pituitary gland</td>
<td>LH (FSH)</td>
<td>Arencephaly</td>
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<tr>
<td>Testis (Leydig's cell)</td>
<td>Testosterone</td>
<td>Pituitary aplasia</td>
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<td></td>
<td></td>
<td>20,22-Desmolase</td>
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<tr>
<td></td>
<td></td>
<td>3β-Hydroxysteroid dehydrogenase</td>
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<td></td>
<td></td>
<td>17-Hydroxylase</td>
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<tr>
<td></td>
<td></td>
<td>17,20-Desmolase</td>
</tr>
<tr>
<td></td>
<td>Dihydrotestosterone</td>
<td>17β-Hydroxysteroid dehydrogenase</td>
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<tr>
<td></td>
<td></td>
<td>Pseudovaginal perineoscrotal</td>
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<tr>
<td></td>
<td>Steroid-receptor complex</td>
<td>hypospadias</td>
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<tr>
<td>Spermatic cord</td>
<td></td>
<td>Testicular feminization</td>
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<tr>
<td>Gubernaculum</td>
<td></td>
<td>Reifenstein's syndrome</td>
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<tr>
<td>Processus vaginalis</td>
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</table>

- canalicular, located between the internal and external inguinal rings; or
- ectopic, located outside the normal pathways of descent between the abdominal cavity and the scrotum (Figure).

The most common site of testicular ectopia is the superficial inguinal pouch of Dennis Browne, although ectopic testes may also be found in suprapubic, femoral, and even perineal sites.18

DIAGNOSIS

It is of utmost importance to differentiate the true undescended testis from the more common retractile testis. This may be a difficult differentiation, particularly in the child over 5 years old. The retractile testis is a benign disorder due to a hyperactive cremasteric reflex; it does not require intervention. It is helpful to review old medical records to determine whether the testes have ever been present in the scrotum. One or more visits to the physician's office may be necessary to differentiate a retractile from a cryptorchid testis. In a relaxed child, a retractile testis usually can be manipulated or milked into the scrotum using gentle traction.

Once a testis is thought to be truly cryptorchid, it is important to verify its position. When located at the superficial inguinal pouch or near the external ring, the testis is usually palpable. When the testis is not palpable, it is usually intracanalicular or intraabdominal.1 With the finding of bilateral nonpalpable testes, it is important to rule out bilateral anorchia. This differentiation can usually be made using a three-day course of HCG (2000 IU daily × 3).19 In the anorchid state, basal gonadotropin levels are extremely high and there is no increase in testosterone levels following exogenous HCG administration.

A unique dilemma is that of the unilateral impalpable testis. It is important to establish its presence so that appropriate management may be undertaken either to put it in a palpable position surgically or to remove it. Ultrasound, CT scanning, MRI, hemiography, and testicular angiography and venography have been used with variable results. More recently the use of the laparoscope has been popularized to locate these testes.20,21 Regardless of the diagnostic test chosen, it is reasonable to assume that all patients with unilateral impalpable testis will require an exploration to determine whether the testis is present or not.
TREATMENT

There is much theoretical and practical rationale for correcting the undescended testis, including: 1) the correction of a cosmetic defect; 2) the potential for psychologic maladjustment that might be prevented or reversed by bringing the testis into the scrotum; 3) an increased susceptibility of the undescended testis to malignant degeneration (if not removed it is certainly wise to place it in a site where it can be palpated with ease); and 4) the potential for improvement of fertility.

It is our policy to surgically place the testis within the scrotum at or around the end of the first year of life. In all prepubertal children, we attempt to salvage all testes if possible and try to place them in a site where they can be easily palpated. If this is not possible, an orchiectomy is performed. Orchiectomy should also be considered for the late postpubertal male and in patients with intersex syndromes in which the testes might be dysgenetic and prone to malignant degeneration.

In most cases, orchiopexy can be performed in an outpatient setting. In unilateral situations, we prefer a standard inguinal incision, whereas in the case of the nonpalpable testis, it may be necessary to enter the peritoneum to search for the organ. For bilateral nonpalpable testes, we prefer a midline transabdominal approach.

At times, the testes cannot be placed easily within the scrotum. Staged operations or actual transection of the cord relying on accessory blood vessels (Fowler-Stephens technique) with or without microsurgical reanastomosis have been used with mixed results to bring such high undescended testes down to the scrotum. 22 Hormonal therapy (HCG and GnRH) has been used for the treatment of undescended testes. HCG administration was proposed under the premise that it would stimulate the Leydig's cells, resulting in an increase in plasma testosterone and thus promoting testicular descent. The results, however, have been less than ideal. 23,24 The results with GnRH are controversial, 25 but in our hands have been very disappointing. 26 In our opinion, the value of hormonal therapy in treating cryptorchidism is still an unresolved issue requiring additional controlled studies. In any event, early therapy (at or before the first birthday) is advocated.

COMPLICATIONS

Hernia/Hydrocele

 Virtually all undescended cryptorchid testes are associated with an indirect hernia. This is due to persistence of the processus vaginalis.

Torsion

The increased susceptibility of the undescended testis to undergo torsion is due to an anatomic discrepancy between the testis and its mesentery. 1 Torsion is most likely to occur in the postpubertal male, when there is a gross increase in testicular size relative to the mesentery.

Infertility

To produce viable and mature spermatozoa, the testis must descend from the warm intraabdominal environment to that of the cool intrascrotal compartment. 27 Even a rise of 1.5° to 2° C greater than that of the scrotum will inhibit spermatogenesis, although the function of the Leydig's cells (testosterone synthesis) is not affected. The further the testes are away from the bottom of the scrotum the greater the likelihood of damage to the seminiferous tubules. Of interest is the fact that the defect in spermatogenic activity of the contralateral scrotal testis may also be present in the patient with unilateral cryptorchidism. 28,29 Lipschultz et al discovered that the unilateral cryptorchid had much lower than expected sperm counts when compared with normal adult patients. 30

Neoplasia

The association between neoplasia and cryptorchidism is controversial. Approximately 10% of testicular tumors arise in undescended testes. 31 The chance of an undescended testis undergoing malignant degeneration is approximately 1 in 4,000 (2.2 per 8,000) each year. Thus the risk of an undescended testis undergoing malignant degeneration is small; however, an abdominal testis is four times more likely to undergo malignant degeneration than an inguinal testis.

Because testicular tumors have occurred in patients who have undergone orchiopexies as early as 5 years of age, we recommend surgical correction around the first year of age, since there is little likelihood of descent beyond this age and ultrastructural changes (abnormalities) begin to occur during the second year of life. 32 Whether early surgical correction will deter the potential for development of neoplasms remains to be seen.

Johnson et al have shown that testicular tumors can also occur in the contralateral scrotal testis of the patient with unilateral cryptorchidism. 33 In bilateral cryptorchidism there is a 15% chance of developing a tumor in the contralateral testis, should one testis become involved with tumor. 34 If both testes are intraabdominal and one testes becomes malignant, there is approximately a 30% chance that the other testis will become malignant. The most common form of tumor in this group is seminoma, followed by nonseminomatous germ cell tumors. In the intersex disorders associated with cryptorchidism, gonadoblastoma is the most common tumor seen. 35

CONCLUSION

Cryptorchidism is a frequently neglected problem