

PediatricsⁱⁿReview[®]

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Pediatr. Rev. 1990;11;305-308

DOI: 10.1542/pir.11-10-305

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Undescended Testis and Orchiopexy: Recent Observations

Charles E. Hawtrey, MD*

The questions below should help focus the reading of this article.

1. What effect does prematurity have on testicular descent?
2. What is the relationship between undescended testes and testicular neoplasia?
3. Are men with treated unilateral undescended testes as likely to be fertile as normal men?

Within the past two decades, observations from a number of sources have expanded our understanding of undescended testes in children. As neonatology has grown, the observations of infants with low birth weight and knowledge of the implications of this condition for undescended testes have also increased. Information obtained from biopsy, including that from studies using electron microscopy, has suggested decreased spermatogonia in children with abdominal testes with age, indicating a need for medical or surgical intervention soon after 1 year of age. The effects of orchiopexy and hormonal manipulations to assure fertility in adulthood have been clarified to the extent that an algorithm for patient management can be constructed.

ANATOMY

An undescended testis has been identified in 0.8% of male infants at 1 year of age¹ and in about 0.2% of adult male military recruits. The incidence rises to 21% in premature neonates weighing less than 2,500 g. Even more striking, nearly 100% of profoundly low-birth-weight neonates (weighing approximately 900 g) exhibit bilateral undescended testes. With weight gain and age, the testes of infants who weighed 900 g at birth proceed toward descent and at 1

year of age have the same incidence as their peers.

Many authors in Europe and the United States have noted that scrotal descent of the testis by 3 years of age preserves spermatogonia, implying a beneficial effect on adult fertility. Electron microscopy now suggests that there are not significant changes in spermatogonia in infants with undescended testes in the 1st year of infant maturation but that, by 5 years of age, there is a significant (60%) reduction in spermatogonia. Data indicating fertility in testes following orchiopexy is limited. Studies in rats clearly demonstrate that pregnancy and fertility can be achieved following surgical correction of an experimentally induced undescended testis.

Low birth weight and prematurity are associated with a higher rate of undescended testis than that of average infants.

Such results have not been achieved in human subjects, and long-term data in human males is limited.

PATHOPHYSIOLOGY

Hormonal Features

During the past 30 years, a number of researchers have investigated the effects of nondescent on spermatogonia, Sertoli cells, and Leydig cell function in the testis. Many of the experimental observations (which would be impossible in human subjects) demonstrate complex hormonal interactions between spermatogonia, sustentacular Sertoli cells, and interstitial Leydig cells. Hormonal manipulations carried out in adult animals have provided insight into the effects of these manipulations on mature cellular elements and the responses of developed cellular compartments of the testis. However, the effects of cryptorchism in adult ani-

EDUCATIONAL OBJECTIVE

84. The pediatrician should have the appropriate ability to counsel parents concerning hormonal therapy for cryptorchism (Recent Advances, 89/90).

mals may be different than those in immature animals. Additional information from studies of prepubertal cryptorchism induced in animals has allowed the conclusion that biofeedback from seminiferous tubular elements helps regulate testosterone synthesis within the testis.

Risks of Neoplasia

There is a significant risk for malignant transformation in the undescended testis. The risk of such transformation in the intraabdominal testis is higher than in the scrotal testis. Some authors suggest that orchiopexy before 5 years of age confers an incidence of neoplasia similar to that of boys without a history of cryptorchism. A family history of cryptorchism and diagnosis of testicular neoplasm in one male child mandates a complete examination of his male siblings because they may harbor a testicular neoplasm or develop one in the future.

There is a significant risk for malignant transformation in the undescended testis.

The incidence of neoplasms found in patients with undescended testes varies from 3% to 18% (mean value 11%). The wide range represents studies with extensive and limited

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Undescended Testis

care numbers. Seminomas predominate as the most frequent type of neoplasm. The contralateral testis (which descended normally) is also at risk for neoplasia, but to a significantly lesser degree. Working with a select population at Sloan-Kettering Cancer Center, Batata et al² report the development of neoplasm in the contralateral testis in 10 out of 125 individuals with undescended testes (8%). This agrees with the results of Johnson's series at Wilford Hall Medical Center, the referral center for the Air Force, in which 8.2% of military recruits with one undescended testis were found to have developed neoplasms in the contralateral, descended testis.³ The mean age for the diagnosis of a testis neoplasm in patients identified or treated for undescended testis is 26 years. Most of these individuals underwent orchiopexy at puberty and demonstrated an average lapse time to neoplastic transformation of 9 years. These data probably are skewed to an older age because at the present time orchiopexy is usually performed before the age of 5 years. Orchiopexy or descent of the testis in response to hormonal therapy should not encourage a false sense of security. Patients should be taught self-examination and encouraged to seek medical assistance if there is a disproportionate increase in consistency or size of either testis.

TREATMENT

Life History of Undescended Testis

About 97% of males have descended testes at birth, and most of those who have undescended testes will experience descent in the 1st year of life. In a review of births in England, a rate of 1.58% for undescended testes at birth was found. Previously, Scorer demonstrated an incidence of only 0.8%. This dramatic difference may be explained practically by recent increases in the number of low-birth-weight infants and infants born with multiple congenital anomalies (which would have been associated with early death in Scorer's series). The clinical observations in the literature indicate that most

affected individuals are identified in childhood and treated with hormonal or surgical manipulations. In many of the survey series of testicular neoplasm, some persons are identified as having undescended testes as adults because they become symptomatic (with neoplasm) or are unable to have children.

Data on the incidence of undescended testis are usually acquired from large-scale studies of young male men (ie, the data used were gathered during military induction physical examinations). In 1940, the study of Gilbert and Hamilton of 9.14 million United States military recruits identified 22 665 individuals with undescended testes (0.25%). In the Netherlands, Velvaardt found only 43 persons with undescended testes among 325 037 recruits, a rate of 0.013%. These observations merely represent a "window" into the absolute incidence of undescended testis, because Velvaardt reports neither the incidence of 17-year-old boys in the Dutch population nor the frequency of 17-year-old boys in a large series of testis neoplasms, and Gilbert reports neither the population of males in the United States in 1940 nor the distribution of recruits in that draft period (which included individuals between ages 17 and 45 years).

There is a cluster of patients who may experience reascent of the testis after initial descent.

An increased incidence of undescended testes from the incidence previously reported is suggested in several sources. Data from several surveys of large numbers of military recruits suggest that the incidence of undescended testes is more prevalent than the 0.8% reported by Baumrucker⁴ and Scorer. Most clinicians accept Scorer's data with the recognition that new treatment for low-birth-weight infants may increase this baseline to 1.5%. The fact that the testis may reascend may also increase the number of boys identified with undescended testes. Pike⁵ has reported that, in one group, 40%

of the boys at 1 year of age demonstrated reascent of testes. This occurred more frequently among individuals with bilateral undescended testes. Atwell⁶ reported 10 patients with complete hernia sacs to the testis who demonstrated reascent of the testis into the inguinal region. These patients required orchiopexy at a relatively late age. One individual was evaluated by testis biopsy and demonstrated decreased spermiogenesis compared to the other testis, which had been involved with a varicocele.

Many techniques have been recommended to identify the undescended testis, including gonadotropin stimulation, venography of the spermatic vessels, laparoscopy, thallium imaging, magnetic resonance imaging, and computerized tomography scanning. All of the radiographic techniques involve more radiation to the undescended gonad than either the thallium scanning techniques or laparoscopy. When an intraabdominal testis is suspected by the presence of a closed external ring and when no palpable testis can be defined, laparoscopy is helpful for identification. Laparoscopy allows identification of chord structures, the testis, and the ductus deferens in the intraperitoneal cavity or chord existing through the inguinal ring, thereby confirming gonadal position in preparation for surgical exploration.

Studies evaluating the fertility of the unilateral undescended testis are few and support the use of orchiopexy well before puberty, which was the accepted practice 30 to 40 years ago. Alpert et al⁷ reported a series of 12 patients, 10 of whom had undergone orchiopexy between the ages of 6 and 15. Only four individuals had

Early medical or surgical treatment is indicated after 1 year of age because the number of spermatogonia declines with increasing age.

sperm in the ejaculate after vasectomy of the normal testis, and these four individuals had sperm counts of 2.2 to 2.9 million sperm/mL of ejaculate. Similarly, Eldrup studied four

patients who had undergone orchiopexy between the ages of 1 and 12 years. Only one patient had a sperm count demonstrating fertility (28 million/mL of ejaculate). Orchiopexy after 8 years of age confers little hope of adult fertility.

Hormonal Manipulations as Treatment

Hormonal manipulations using human chorionic gonadotropin to induce descent of unilateral and bilateral undescended testis have been reported by several investigators. In their combined series, Albescu et al⁸ and Knorr⁹ reported fertility in 25 (53%) of 47 individuals with bilateral undescended testes and in 23 (43%) of 54 with unilateral undescended testis treated with human chorionic gonadotropin alone. Two excellent double-blind controlled studies^{10,11} of human gonadotropin and gonadotropin-releasing hormone therapies have demonstrated essentially equal effectiveness, inducing testicular descent at rates of 6% to 19%. Spontaneous testis descent occurred in 8% of those patients studied. The controlled studies indicate no clear benefit of human chorionic gonadotropin or gonadotropin-releasing hormone in truly undescended testes. These rigidly controlled studies also suggest that human chorionic gonadotropin or gonadotropin-releasing hormone could be helpful to patients with retractile testes: A group of 5 boys with retractile testes all responded to human chorionic gonadotropin, although some patients did not respond completely and subsequently underwent orchiopexy.

The retractile testis responds well to hormonal therapy.

Treatment regimens vary, but they generally take 2 to 5 weeks. Injections may be given on alternate days or twice weekly. Gonadotropin-releasing hormone treatments are given by intranasal inhalation, in doses of 1.2 mg/day (200 µg given at 2-hour intervals, or 6 times per day) for 4 weeks.

Surgical Manipulations

Orchiopexy has been offered as a means of ensuring fertility in adulthood and reducing the risk of malignancy, which has a latency of as long as 20 years. Other benefits include the preservation of hormone function and scrotal placement of the testis, which allows easy examination. Orchiectomy may be advised in older children (8 to 14 years of age) who have a normal-sized testis on the opposite side. Subtle factors, such as body image and testicular prostheses, require compassionate counseling for boys who choose orchiectomy.

Johnson, Altman and Grand Gehringer have advocated orchiopexy before 6 years of age, based on their observation that, of 49 patients, a patient who underwent orchiopexy at the age of 5 years was the only one to develop a neoplasm. In fact, all authors presently recommend early orchiopexy. However, the effects of testicular neoplastic latency for early orchiopexy (age 2 to 3 years) are not yet reflected in the literature by data from a sample followed into adulthood, and the current published data still reflect the previous recommendation that surgeons should wait to see the effects of puberty on testicular descent before performing orchiopexy.

Surgical techniques offer a variety of styles of management. The avoidance of tension on the testis and chord structures represents one of the cardinal principles of any method of repair. Although surgical techniques for accomplishing the scrotal location of the testis vary, common principles include (a) isolation and ligation of the hernia sac; (b) free mobilization of the chord with its vascular and vasal components for tension-free placement in the scrotum; (c) placement of the testis in an environ-

Surgical treatment requires close attention to details of technique.

ment free of surrounding fat so that testicular maturation can occur; (d)

placement of the testis in the scrotum by the most direct route possible; and (e) recognition that the testis has a dual blood supply from the gonadal vessels and the vasal artery, both of which contribute to gonadal nutrition.

The dartos pouch technique, either ipsilateral or contralateral, provides fixation of the testis. The Ombredanne and Torek procedures emphasize ligation of the hernia sac and adequate cord length. The Prentiss and Fowler-Stephens operations stress the importance of chord mobilization and straight-line placement of the testis in the scrotum. Microvascular anastomosis and the Fowler-Stephens procedure are required for intraabdominal testes manifesting a short spermatic vascular pedicle.

Clearly, a number of factors influence the treatment of the undescended testis. Hinman¹² has taken the controversial view that some patients with severe congenital anomalies associated with undescended testes do not require therapy for their undescended testes. Caution must be exercised in this area. Some children with congenital anomalies who in the past would have died at an early age now survive into the age group at risk for testis neoplasia.

The absence of a ductus deferens may be overcome by vaso epididymostomy and transplantation of the testis across the scrotal septum. Most surgeons advocate the principles espoused by Levitt, which call for the preservation of gonadal tissues and orchiopexy before the age of 5 years.

Data regarding fertility are available from several sources. Data collected from Kogan suggest that the incidence of azoospermia is greater than 71% of persons treated for bilateral cryptorchism and 49% among men treated for unilateral undescended testis¹³.

Hormonal manipulations are most successful in patients with bilateral undescended testes. Orchiopexy has been useful in patients with unilateral undescended testes, bilateral undescended testes unresponsive to hormonal manipulation, and individuals with high intraabdominal testes. This latter group is best treated with vascular anastomosis using the inferior epigastric artery and vein. An algo-

TABLE. Algorithm for Management of Undescended Testes

At birth:	
Multiple congenital anomalies	Assess anomalies and give priority to those that threaten life
Ambiguous genitalia	Karyotyping Genitogram Gonadal biopsy Panendoscopy Surgical management
After 1 y of age	
Bilateral undescended	Counsel family
Palpable testis	Hormonal stimulation
Manipulable testis	1500 IU human chorionic gonadotropin/M2 2 times per wk for 2 to 5 wk 1.2 mg of gonadotropin-releasing hormone given intranasally (response probability of 6% to 19%) Orchiopexy if response to hormonal therapy is limited or absent
Bilateral maldescent (nonpalpable)	Diagnostic localization Laparoscopy to identify chord structure or intra-abdominal testes
Open external ring	Human chorionic gonadotropin stimulation Orchiopexy if hormonal stimulation fails
Unilateral undescended	Counsel family
Palpable testis	Hormonal stimulation
Manipulable testis	1500 IU human chorionic gonadotropin/M2 2 times per wk for 2 to 5 wk or intramuscularly daily for 28 d Orchiopexy if response to hormonal therapy is limited or absent
Unilateral maldescent (nonpalpable)	Diagnostic localization Laparoscopy Thallium scan Computed tomography or magnetic resonance imaging
Testis reascent	Orchiopexy
Unilateral undescended (after 1 y of age)	Orchiopexy Counsel family regarding: Decreased likelihood of fertility Continuation of hormonal function Increased likelihood of testicular dysgenesis at or near puberty, at which time orchiectomy becomes an option

Algorithm for the management of children with undescended testis is outlined in the Table.

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Self-Evaluation Quiz

11. Which of the following is least likely to be a true statement?

- A. 0.8% of 1-year-old boys have an undescended testis.
- B. 0.2% of male military recruits have an undescended testis.
- C. Over 20% of premature male infants weighing less than 2500 g have an undescended testis.
- D. A very premature 900-g male newborn with bilateral undescended testes is unlikely to have descended testes at 1 year of age.
- E. Most individuals with undescended testes are identified in childhood.

12. Each of the following is a true statement pertaining to testicular neoplasms, except:

- A. About 11% of males with undescended testes develop neoplasms.
- B. Orchiopexy reduces the risk of testicular neoplasia to no more than that of the normal population.
- C. Seminomas are the most frequent type of testicular neoplasm.
- D. 8% of men with an undescended testis develop a neoplasm in the contralateral testis.
- E. The risk of malignant transformation in an undescended testis is higher for an intra-abdominal testis than for a scrotal testis.

13. Which of the following is least likely to be a true statement?

- A. Over 70% of men treated for bilateral cryptorchidism have azoospermia.
- B. Men treated for unilateral undescended testes are as likely to be fertile as men with bilaterally normally descended testes.
- C. Medical or surgical treatment for undescended testes is best done at about 1 to 2 years of age.
- D. Controlled studies show no clear benefit of hormonal treatment of truly undescended testes.
- E. Appropriate surgical treatment of undescended testes requires close attention to details of technique.

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