Absent or Non Descent of the Testis

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1. Introduction

Cryptorchidism is a common congenital anomaly of newborns that may resolve, persist or first appear in later childhood. It affects 4% to 5% of full-term and in 9% to 30% of premature males at birth. This figure falls to around 1% to 2% after 3 months, as a significant number will descend spontaneously within the first few months of life (Barthold, & Gonzalez, 2003, Sijstermans, et al. 2008)

The testis can be found in any position along its usual line of descent; however, approximately 80% will be located in the inguinal region, just outside the inguinal canal. Approximately 20% of undescended testes are nonpalpable, and in 20% to 50% of children with nonpalpable testis, the testis is absent (Smolko& Brock, 1983)

Laparoscopy has been established as the most reliable diagnostic modality for the management of impalpable testes, It clearly demonstrates the anatomy and provides visual information upon which a definitive decision can be made. Non visualization of the testes at laparoscopy has been coined with the broad term (Absent testis), which is coined with vanishing, atrophied or agenetic testes.

In this report we will discuss the phenomena of absent testes in the light of recent discovery of a subgroup of testes that failed to descend from it is embryological subrenal position and likely to be labelled as an absent testis unless one is aware of the complexity of testicular development and descent

2. Testicular development and descent

Proper evaluation and management of cryptorchidism requires a thorough understanding of the normal testicular development and descent which depend on a complex interaction among endocrine, paracrine, growth, and mechanical factors.

Bipotential gonadal tissue begins differentiation into a testis during the 6th and 7th weeks of gestation under the effects of the testis-determining SRY gene. At the eighth week of gestation, Sertoli cells appear and produce Müllerian inhibitory substance (MIS) to cause regression of the Müllerian ducts. By the 10th week, Leydig cells produce androgens and insulin-like factor 3 (INSL3). Androgens are important for differentiation of various parts of the Wolfian duct and both androgens and INSL3 are required for testicular descent (Hadziselimovic & Adham, 2007; Hutson & Beasley, 1988)

Development of the male external genitalia, including the scrotum, occurs between weeks 10 and 15 of gestation and results from the conversion of testosterone to dihydrotestosterone
by the enzyme 5 alpha reductase type 2 in the primordia of these tissues. The development of the scrotum allows for the ultimate descent of the testis from the abdomen.

2.1 Wolffian duct development
The Wolffian duct is originally derived from the pronephros, whose ductal derivative elongates posteriorly through the mesonephros and extends to the cloaca. The pronephros eventually degenerates but its ductal derivative remains in the mesonephros and becomes the Wolffian duct (WD). WD structure is further differentiated into epididymis, vas deferens, seminal vesicle and ejaculatory ducts, and is dependent on androgens from fetal Leydig cells for its development. The anterior or upper portion of the WD adjacent to the testis elongates and folds into the epididymis. Meanwhile, the mesonephric tubules differentiate into efferent ducts that eventually connect to the rete testis and the epididymis. The middle portion of the WD remains a simple tube, to form the vas deferens. The posterior or caudal portion of the WD dilates, elongates cranially and eventually forms the seminal vesicle (Hadziselimovic et al., 1987; Hutson & Beasley, 1988; Saino et al. 1997)

Androgens are crucial for the maintenance and elaboration of the WD later in development. Their action is mediated via their receptor in the androgen receptor (AR) inside target cells. Androgens enter their target cells and bind to AR to regulate the transcription of specific genes. In humans, androgen insensitivity syndrome owing to null mutations of AR resulted in the female phenotypes (Hadziselimovic & Herzog, 2001; Wensing, 1988). Furthermore, when females were exposed to excessive androgens by testis transplantation during fetal development, the WD persisted, signifying the role of androgen in WD development (Hadziselimovic & Adham, 2007; Rajfer & Walsh, 1977).

2.2 The gubernaculum development
The gubernaculum undergoes 2 phases of development. In the first phase the gubernaculum thickness, in a process known as the swelling reaction, which is mediated primarily by Insl3. This process dilates the inguinal canal and creates a pathway for testicular descent. The first phase of descent is complete by 15 weeks of gestation. During the second phase the gubernaculum undergoes cellular remodeling and becomes a fibrous structure rich in collagen and elastic fibers. At about the 25th weeks of gestation the processus vaginalis elongates within the gubernaculum creating a peritoneal diverticulum within which the testis can descend. A central column of gubernacular mesenchyme remains attached to the epididymis. Gubernaculum then bulges out of the abdominal musculature and begins to elongate towards the scrotum, eventually arriving there between 30 and 35 weeks of gestation (Shenker et al., 2006; Wensing, 1988)

Failure of the first phase of descent is rare and results in an intraabdominal undescended testis (UDT). Failure of progression of the second stage of descent is more common, and the UDT remains somewhere between the internal inguinal ring and the neck of the scrotum. It should be noted that the gubernaculums does not provide any traction on the testis to cause its descent nor is anchored to the scrotum, but mainly attached to the epididymis. Under androgen stimulation the gubernaculum pulls the epididymis and facilitates its descent, indirectly guiding the testis into the scrotum. (Hadziselimovic, 2001, 2007)

In addition, the epidermal growth factor plays an active role at the level of the placenta to enhance gonadotropin release, which stimulates the fetal testis to secrete factors involved in descent such as descendin, an androgen-independent growth factor involved in gubernacular development. (Hadziselimovic & Adham, 2007)
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Other mediators of descent include calcitonin gene-related peptide (CGRP). It is excreted by the genitofemoral nerve under androgen stimulation. It causes contraction of cremasteric muscle fibers and subsequent descent of the gubernaculum, followed by the testis. (Hutson & Beasley, 1988; Shenker et al. 2006)

Both (MIF) and testosterone act locally as paracrine hormone. Failing of the testis to secrete the MIF hormone will lead to ipsilateral persistent of mullerian tissues and abnormality of the paracrine function of testosterone is responsible for epididymal anomalies and UDT (Husmann & Levy, 1995; Shenker et al., 2006)

There are animals in which the epididymis descends and the testis remains intra abdominal, but there are no animals in which the testis descends and epididymis remains intra-abdominal a crucial information in understating laparoscopic finding of impalpable testes (Hadziselimovic & Adham, 2007)

If the testis is agenetic, one would expect that the ipsilateral mullerian structure not be suppressed. The absence of Mullerian remnants means that the there has been a testis at one stage of development that survived well above the 9th week of gestation.

2.3 Processus vaginalis

The processus vaginalis grows along and partially encircles the gubernaculum, creating a potential space in the inguinal canal and scrotum. Although the testis is stationary between the 3rd and 7th months of fetal life, the gubernaculum and the processus vaginalis together distend the inguinal canal and scrotum, thus creating a “path” for testicular descent.

2.4 Testicular agenesis

A testis may be unable to form in a 46, XY individual because the gonadal ridge fails to form or its blood supply fails to develop. Individuals with testicular agenesis may have either a male or a female phenotype. The variable phenotypic appearances, including the presence of some form of the internal genitalia, relate to the time during gestation when the testis was lost. The key clinical sign indicating testicular agenesis rather than a vanished testis is the presence of ipsilateral Mullerian structures. This entity is totally different from the vanishing testis syndrome. It is virtually impossible to have a testicular agenesis in a normal phenotype male with no remnant of mullerian structures on the affected site.

3. Management of impalpable testes

3.1 Imaging of impalpable testes

When the testis is not clinically palpable, a battery of imaging investigations are described to locate the testis. These include ultrasound scanning (USS), magnetic resonance imaging (MRI), magnetic resonance angiography (MRA) and Computed tomography (CT). Despite these many options, it is still commonly believed that none of them accurately predict either the position or morphology of the testis, with the overall accuracy of radiological investigations being estimated at only 44%. (Fritzsche et al. 1987, Kullendorff et al. 1985, Malone & Guiney, 1985; Weiss, 1979, 1986)

However there are occasions in which imaging is undoubtedly beneficial especially in obese children where although a testis appears to be impalpable following clinical examination; it can be located either intracannicular or at superficial inguinal pouch position by simple US. These patients can then proceed to inguinal exploration with the option to convert to laparoscopy if no testis was found. Although some centers still advocate groin exploration in impalpable testes.
several studies have shown that a significant proportion of testes that appear absent at the time of inguinal exploration can subsequently be identified at laparoscopy. (Boddy et al., 1985; Patil et al., 2005; Perovic; Janic 1994)

### 3.2 Laparoscopy for impalpable testes

Laparoscopy has been established as the most reliable diagnostic modality for the management of impalpable testes. In experienced hands, laparoscopy is capable of providing nearly 100% accuracy in the diagnosis of the intra-abdominal testis with minimal morbidity. It clearly demonstrates the anatomy and provides visual information upon which a definitive decision can be made. Both internal rings can be inspected; the location and size of the testes, their blood supply and the nature, course and termination of the vas, and epididymis can be determined. All of these anatomical landmarks individually or collectively have bearing on the operative management of the Impalpable testes. (Atlas & Stone 1992; Bianchi, 1995; Bogaert et al. 1993; Elder, 1993; El Gohary, 2006; Froeling et al. 1994; Humphrey et al. 1998; Poenaru et al. 1994; Perovic & Janic 1994)

In our series of 1652 UDT seen between 1986-2009, 431 were impalpable representing 26.5%. We used both diagnostic and/or operative laparoscopy in the management of 362 testes from 1992 to 2009. Table 1 depicts our updated figures of laparoscopically managed UDT

<table>
<thead>
<tr>
<th>LAPAROSCOPIC FINDING OF IMPALPABLE TESTES (362)</th>
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<tr>
<td>Vanishing testis</td>
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<tr>
<td>Atrophic Abdominal</td>
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<tr>
<td>Atrophic Scrotal</td>
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<tr>
<td>No vas</td>
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<td>Superficial inguinal pouch</td>
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<td>Canalicular</td>
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<td>Abdominal</td>
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<th>ABDOMINAL TESTES (170)</th>
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<tr>
<td>High Abdominal</td>
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<tr>
<td>Above ring</td>
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<tr>
<td>Subrenal</td>
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<td>Persistent Müllerian</td>
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<td>Spleno Gonadal Fusion</td>
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<th>OPERATIVE PROCEDURE FOR ABDOMINAL TESTES</th>
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<tr>
<td>FSO</td>
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<td>One Stage Lap. Orchedopexy</td>
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The possible findings at laparoscopy is either a normal testes at variable distance of the closed or opened internal ring atrophied or no testes. Fig 1-4. If no testes are identified, one is left with the possibility of vanishing or absent testes. Vanishing abdominal testes are readily diagnosed when a blind-ending vas meets a leach of flimsy testicular vessels, and are thought to result from a prenatal vascular accident or intrauterine testicular torsion (Stephen & Lawrence, 1986) Fig 3. Intra-abdominal testicular torsion as a cause for testicular atrophy or vanishing testes has been postulated but as far as we can ascertain never been
seen. However one of our patients aged 8 had an atrophied left testis due to several twists of its blood supply leading to atrophic changes (Fig 4) (El Gohary, 1997)

Fig. 1. Testis near opened internal ring

Fig. 2. Testis away from closed internal ring
Fig. 3. Vanishing testis

Fig. 4. Atrophied testis with vascular twist

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3.2.1 Testicular epididymal separation
As the vas is embryologically derived separately from the testis (Hadziselimovic, et al. 1987), finding the vas alone with no testicular vessels does not exclude an existing testis in abnormal locations or merely separated from the vas. Testicular epididymal separation allowing epididymis to elongate and descent to the scrotum without associated testicular descent is a known phenomena (Marshall & Shermeta, 1997; Shereta, 1979) Fig 5, but there are rare situation of complete urogenital nonunion in which there are no communication between the descended epididymis and the UDT. (Emanuele, 1997; Wakeman, 2010; El Gohary, 2009). An extreme example of this was one of our reported cases in which the vas enters closed internal ring and a normal testis lying completely dissociated from the vas in the pelvis (El Gohary, 2009) Fig 6. This particular case would have been labeled as an atrophied testis, but for the diagnostic accuracy of laparoscopy. The explanation to these phenomena is related to the embryological development of the wolfian system separately from the testis with the gubernacular attachment to the epididymis rather than the testis. (Hadziselimovic, 2007)

![Separated epididymis](image)

**Fig. 5.** Separated epididymis (vas is seen entering the canal leaving an intra-abdominal testis)

3.2.2 The testicular vessels as a landmark for testis
The testicular vessels are a good landmark for testicular localization and there is a relationship between the size of the feeding vessels and the testicular tissue. (El Gohary, 1997; Smolkó 1983) Visualizing of well developed spermatic vessels predicts the presence of a good-sized testis whereas poor blood supply is invariably associated with poorly developed or atrophied testes (fig 7,8)
Fig. 6. Urogenital non-union

Fig. 7. Normal size testicular vessels and vas deferens entering closed ring
Obese boys with UDT are difficult to examine even under GA. Those group of patient may benefit from an initial ultrasonography and groin exploration before embarking upon diagnostic laparoscopy. These children represent the majority of our patient subjected to diagnostic laparoscopy with the finding of good testicular vessels leading to a good size testes outside abdominal cavity during groin exploration.

3.2.3 Absent testes
The term absent testes has been used in the literature to denote vanishing, atrophied, nubbin of tissue at the end of the spermatic or agenetic testes. Agenetic testes in a 46, XY individual do occur because the gonadal ridge fails to form or its blood supply fails to develop. Individuals with testicular agenesis may have either a male or a female phenotype. The variable phenotypic appearances, including the presence of the internal genitalia, relate to the time during gestation when the testis was lost (Shenkeret al. 2006). The key clinical sign indicating testicular agenesis rather than a vanished testis is the presence of ipsilateral Müllerian structures. True congenital absence of one testis is virtually impossible in a phenotype male with no remnant of mullerian structures on the affected site.

3.2.4 Non-descent of the testes
Non-descent of the testes is a subgroup that may cause confusion about the real status of the testes. They are located at their initial embryological position below the kidneys, in contrast
to the high abdominal testes which are present along the line of descent at a variable distance from the internal ring (fig 2). This entity was realized when, during routine laparoscopy for impalpable testes, a leash of flimsy vessels was encountered entering an open inguinal canal with no vas (Fig. 9). The initial impression was that of an absent testis. During further inspection a vas was found hidden under the caecum and going in an upward direction toward the right hypochondrium. When followed the vas was seen to join the epididymis which was attached to a subrenal testis (Figs. 10 and 11). In 2008 we reported eight testes in 7 patients found at the sub-renal position after an initial finding of no testes and no vas at the pelvic inspection; seven on the right side and 1 on the left. The later belong to a patient with bilateral UDT (El Gohary, 2008). We have since found another 4, all were on the right side. The predominance of right side for this particular cases is difficult to explain and it is rather early to generalize before we collect more cases.

The etiology might be attributed to poorly developed or absent gubernaculum. This is highlighted by the fact that the only trace of gubernacular tissues in the present cases was a leash of vessels along the course of testicular descent. Gubernaculum is attached to the epididymis and plays an integral part in testicular decent. There are 2 reports of subrenal testes with initial finding at laparoscopy very similar to our cases, but with the difference that they had no vas or epididymis and associated with ipsilateral multicycstic kidney. There is a correlation between absent vas and renal anomalies (Deane & May, 1982; Ellsworth & Cheuck, 2009; Kim et al. 2005) but those cases of absent vas
Fig. 10. Vas looping up towards subrenal testis

Fig. 11. Vas joining sub-renal testes
and non visualization of the testis are extremely rare. And in patients with normal male phenotypic appearance warrant through laparoscopic exploration to locate the hidden testes along the course of descent.

3.2.5 Spermatic vessel ligation
In 1903, Bevan suggested division of the spermatic vessels to allow for scrotal placement of high abdominal testes. Fowler and Stephens, 1959 expanded on this approach by dividing the spermatic vessels well above the testis and carefully preserving the collateral vassal arteries by leaving a strip of peritoneum attached to the vas when dissecting it into the pelvis. Ransley et al. 1984 reported a two-stage Fowler Stephen orchedopexy (FSO); This involved preliminary ligation of the spermatic vessels and after an interval of several months to allow for compensatory dilatation of collateral blood supply. Bloom, 1991 described performing the first stage laparoscopically. Lindgren et al. 1999 reported on laparoscopic single-stage FSO. Although it has been proposed that a single-stage FSO is more favorable than 2stage procedure, as it avoids repeat anesthesia and the potentially difficult dissection associated with re-operation, (Boddy, 1991; Docimo, 1995); The majority of published series favors two-stage procedure as it allows for compensatory dilatation of collateral blood supply and have a better chance for testicular vascularization (Bloom, 1991; Boddy et al.1991; Daher et al. 2009; Dave et al. 2009).

The blood supply to subrenal testes are very short and cannot be mobilized to gain enough

Fig. 12. 2nd stage FSO in a patient with subrenal testis showing good vasculature (clips are close to the testis as the blood supply in subrenal travels short distance)
length of the cord, but the vas runs a log course in upward direction and its blood supply can be used as a support for the mobilized testis using FSO. We have used one stage FSO in 2 patients, one of them became atrophied and the other attained good scrotal position. Two stage Fowler Stephen were used in the management of 10 subrenal testes with good result in 7, (Fig 12) one reached to mid scrotal position and 2 atrophied. The overall success rate for all Fowler-Stephens procedures was 85%, (Daher et al. 2009; Dave et al. 2009; Hutson & Clarke, 2007)

4. Conclusion

When no testis could be identified during laparoscopy, the vas and the testicular vessels are traced as leading points for testicular localization. As the vas develops separately from the genital ridge; its absence does not exclude the presence of a testis in an unusual location. Testicular vessels proved to have high accuracy as a landmark for the developing testis and its size has a relationship with the fictional testicular tissues, however poorly developed gubernaculums can easily be mistaken for hypoplastic testicular vessels. Subrenal none descended testes represent a variant of abdominal testes that are likely to be missed unless one is aware of its possible anatomical location. In this subset of cases there are no vas at initial laparoscopy and what looks like flimsy vessels represent poorly developed gubernaculum. Based upon embryological facts of testicular development, in a phenotypically normal male it is virtually impossible to be associated with an absent or agenetic testis. The absence of Mullerian remnants means that the there has been a testis at one stage of development that survived well above the 9th week of gestation. There are reported cases in which the testis was absent during initial laparoscopy and was subsequently found under the renal lower pole; which makes laparoscopic examination of the site of origin below the kidneys an essential step in all cases apparent absent testes. We do believe that testicular absence does not exist in normal males and that cases that were labeled as (absent testes) should be re-scoped to exclude sub-renal testes. An algorithm for management of impalpable testes is highlighted.
5. References


Kim, C; Baneet, N; & Docim S; (2005) Missed testis on laparoscopy despite blind ending vessels and closed processus vaginalis. Uro 65:1226.e7–1226.


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The present book, published by InTech, has been written by a number of highly outstanding authors from all over the world. Every author provides information concerning treatment of different diseases based on his or her knowledge, experience and skills. The chapters are very useful and innovative. This book is not merely devoted to urology sciences. There are also clear results and conclusions on the treatment of many diseases, for example well-differentiated papillary mesothelioma. We should not forget nor neglect that laparoscopy is in use more extensively than before, and in the future new subjects such as use of laparoscopy in treatment of kidney cysts, simple nephrectomy, pyeloplasty, donor nephrectomy and even robotic laparoscopy will be researched further.

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