

TESTICULAR DESCEND, HOW AND WHY: A REVIEW ARTICLE

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ABSTRACT Background: The testis develops in the dorsal abdominal wall, and then descends to the scrotum. The development begins as early as the 6th week of intrauterine life and is completed by the fifth month of intrauterine life. The testis may get arrested during its descent from dorsal abdominal wall to the scrotum. The anomalies of descent include cryptorchism (and its variant like anarchism, monarchism or partially descended testis), ectopic testis, persistent processus vaginalis and encysted hydrocele of the spermatic cord, and others. Cryptorchism is usually diagnosed during the newly born examination. The recognition of this condition, identification of associated syndromes, proper diagnostic evaluation and timely treatment by a surgical urologist is important to prevent adverse consequences like sterility, congenital hernia & hydrocoele, testicular carcinoma, and others. **Objectives:** The objective of this review is to study the role of gubernaculum in the testicular migration process. **Material & Method:** We performed a descriptive review of the literature about the role of the gubernaculum in testicular migration during the human fetal life. This article provides an overview of the role of gubernaculum and other factors responsible for gonadal migration. **Results:** In the first phase of testicular movement the gubernaculum enlarges to hold the testis near the groin and in the second phase the gubernaculum migrates across the pubic region to reach the scrotum. The proximal end of gubernaculum is attached to the testis and epididymis. The lower end reaches to the bottom of the scrotum. A failure in the proper functioning of gubernaculum causes cryptorchism. Rarely male gonads may deviate from primary pathway due to the presence of many tails of distal gubernaculum, and it may give rise to the ectopic testis. The processus vaginalis usually closes by birth. If it remains patent, it leads to a congenital hernia, hydrocele and encysted hydrocele. **Conclusion:** the gubernaculum presents a significant structure during testicular migration, and its failed mechanism gives rise to different pathological conditions.

KEYWORDS testicular descend, gonads, gubernaculum, processus vaginalis, undescended testis, congenital hernia/hydrocele

Introduction

The urinary system consists of Kidney, Ureter, Urinary bladder and Urethra. The genital system consists of external and internal genitalia. Male internal genitalia is testis, vas deference or ejaculatory ducts and seminal vesicles, whereas the external genitalia is scrotum and penis. The female genital system consists of ovary, uterus and vagina. The testis is male, and ovaries are female gonads. The main difference lies in the fact that the male gonads have a well differentiated ductal system. The duct system is suppressed in the female, and germ cells develop on the surface of female gonads.

The urogenital system develops from urogenital mesoderm.

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Soon after the formation of three germ layers, the mesoderm layer is divided into several parts i.e. axial, paraxial, intermediate and lateral plates. This intermediate mesoderm gives rise to urogenital system. [1] The testis develops before birth in the dorsal abdominal wall. During the human fetal period, the testis migrates from the abdomen to scrotum traversing the abdominal wall and the inguinal canal between 15th to 28th-week post conceptions. The development of gubernaculum is the single most important structure in the testicular migration process. The gubernaculum is a cylindrical structure, covered by the peritoneum from all the sides except posteriorly, where the testicular vessels and vas deference passes to it. The proximal portion of the gubernaculum is adherent to the lower pole of the testis and the epididymis. During testicular migration, these structures move through the inguinal canal as a single unit. During the 8th month it reaches the superficial inguinal ring, and during the 9th month, it comes to rest at the bottom of the scrotum. In the scrotum it bulges into the lower part of the processus vaginalis, causing the invagination of the posterior wall of processus vaginalis.

The factors which contribute to the descent of testis includes Gubernaculum testis, the differential growth of abdominal wall, intra abdominal pressure and temperature, Calcitonin gene related peptide(CGRP), male sex hormones, insulin like hormone 3(INSL3) and maternal gonadotrophins. The descent of testis may become erratic and gives rise to undescended testis, ectopic testis, congenital hernia and hydrocoele etc. This paper discusses the process of migration, the role of Gubernaculum and consequence of the failure of this mechanism.

1. Testicular migration

The testis develops before birth in the dorsal abdominal wall. The development begins as early as 6th weeks of intrauterine life and is completed by the 5th month of intrauterine life. [2] Testicular migration is a complex process wherein the testis migrates from its abdominal position to bottom of the scrotum. [3] During the human foetal period, the testis migrates from the abdomen to scrotum traversing the abdominal wall and the inguinal canal between 15th and 28th-week post conception (WPC). [4-5]

1.1 Intrauterine events

In the early months of the intrauterine life, the scrotum is rudimentary. It has no cavity and testis is high-up on the posterior abdominal wall. Testicular migration happens in two distinct phases. The first phase corresponds to the testicular migration from the abdomen to the internal inguinal ring. Moreover, the second phase corresponds to the transposition of testes through the inguinal canal until their definite arrival at the scrotum. [6]

The exact timing of the testicular migration is controversial. Various authors have quoted this from as early as a 17th week up to a 24th week, but it is more agreed upon that the passage of testis through inguinal canal occurs very quickly.

1.2 The development of gubernaculum The development of gubernaculum is the single most important anatomical structure in the testicular migration process. Using contraction and shortening, it imposes traction forces on the testis. The gubernaculum starts to develop in the human foetus during the 6th week of gestation, the same period when the germinative cells are arriving at the genital ridge. [7-8]

In the 8th week of gestation, the testis and mesonephros are linked to the posterior abdominal wall by a peritoneal fold. As the mesonephros degenerates, a portion of this fold, cranial to the testis, called the diaphragmatic ligament, also degenerates; it then turns in to the cranial position of the gonadal mesentery. This structure is known as the caudal gonadal ligament, which gives rise to gubernaculum testis. Cranially the gubernaculum approaches the mesonephric duct, while distally it approaches the inguinal region. At this moment, the future inguinal canal is still only space in the musculature of the anterior abdominal wall, where only mesenchymal tissue exists.

The gubernaculum is a cylindrical structure, covered by the peritoneum from all the sides except posteriorly where the testicular vessels and vas deference passes. Macroscopically it looks like Wharton's jelly of the umbilical cord. Histologically it is composed of undifferentiated cells with elongated shapes, surrounded by large quantities of extracellular material. It is impossible to identify smooth or striated muscle cells in it, except in its distal end and the peripheral portion. [9] The genital branch of the genitor-femoral nerve, provides, the nerve supply to gubernaculum.

Around the 8th week of gestation, a portion of epithelium starts a small invagination from the coelomic cavity, across from the gubernaculum, slowly penetrating its mesenchymal structures. This invagination occurs bilaterally and is considered as a start of the vaginal process. The growth of the vaginal process divides the gubernaculum into three parts:-

- 1). The main gubernaculum, which corresponds to the portion covered by the visceral layer of the peritoneum of the vaginal process.
- 2). The vaginal gubernaculum- which corresponds to the portion that externally surrounds the parietal portion of the vaginal process.
- 3). The infra vaginal gubernaculum that corresponds to the caudal portion of the gubernaculum which has not been invaded by the vaginal process. [10-11]. Both the gubernaculum and vaginal process change in harmony during testicular migration. The maintenance of this undifferentiated mesenchyme along the inguinal canal and scrotum is essential for the downward extension of the vaginal process to occur, during which it follows the pathway, created by the dilatation of the gubernaculum, forming the canal, through which the testis will reach to the scrotum.

1.3 Proximal gubernaculum

The proximal portion of the gubernaculum is adherent to the lower pole of the testis and the epididymis, during testicular migration these structures move through the inguinal canal as a single unit. According to Johansson and bloom, [12] in this situation the proximal gubernaculum always adheres to the end of the vaginal process. Many studies have shown that the changes in the proximal insertion of the gubernaculum are associated with epididymal anomalies and can contribute to the occurrence of cryptorchism. [13] The proximal portion is necessary by uniting the scrotal region and serving as a guide for testicular migration. Not only that, but it also limits the mobility of testis and prevents testicular torsion.

1.4 Distal gubernaculum

The insertion site of the distal gubernaculum is one of the factors involved in testicular ectopia. [14] Many studies have shown that the distal gubernaculum has six tails or extensions. i.e. abdominal, pubo-penile, femoral, perineal, contra lateral scrotal and scrotal.[15-16] It is speculated that these tails of the gubernaculum exists during the beginning of the foetal development and disappears during testicular migration. If any of these extensions of the distal portion exists, the individual may develop testicular ectopia. [16] The most accepted theory to explain testicular ectopia are:-

- 1). Failure of gubernaculum to dilate the inguinal canal, enabling the testis to migrate through other pathways and not to the scrotum.
- 2). Invasion of the gubernaculum by abdominal wall fascia near the inguinal canal, blocking the passage of testis to the scrotum and diverting it to ectopic sites.
- 3). The existence of multiple distal insertions of the gubernaculum testis, guiding the testis to ectopic sites. So the most accepted theory to explain testicular ectopia is the existence of multiple distal insertions of the gubernaculum.

1.5 The process of testicular migration

The different parts of the gubernaculum undergo various changes during the testicular migration. The vaginal and infra vaginal portion become proportionately longer as the testis starts to descend into the scrotum. Their diameter also increases which helps to dilate the inguinal canal and to allow testis to pass through it. The growth of the gubernaculum can be divided into two phases. In the first phase, its volume increases and the second phase, it decreases in size, coinciding with the complete descent of the testis. [17] The cremaster muscle presents structural alterations during this period as well. The rhythmic contraction of this muscle guides the testis into the scrotum.

The first phase is characterised by the pronounced cell multiplication and accumulation of glycosaminoglycans, mainly hyaluronic acid. These substances act as hydrophilic agents and raise the quantity of water. There is also increase of extracellular material. The presence of myoblast intensifies, and there are changes in the number and arrangement of the collagen fibre and alteration in the elastic system.

In the second phase, the gubernaculum shrinks, particularly in length, frequently accompanied by the descent of the testis. This phenomenon appears to be androgen dependent and brings substantial degradation of the glycosaminoglycans previously accumulated in the extracellular material, with resulting dehydration of this space and condensation of the gubernaculum. Understanding the relationship between regression of the gubernaculum and descent of testis is vital to the comprehension of, how androgens control testicular migration. Studies have demonstrated the association of deficiency of androgens to failed regression of gubernaculum and thus leading to cryptorchism. [18-19]

During the 8th month it reaches the superficial inguinal ring, and during the ninth month, it comes to rest at the bottom of the scrotum, where it bulges forward into the lower part of the processus vaginalis and invaginates the posterior wall of the processus. Two layers of it now cover the testis. The coverings are called tunica vaginalis having outer parietal layer and inner visceral layer. Since the testis

invaginates the processus vaginalis, from the posterior aspect, the posterior border is not covered by tunica.

The orifice of communication between the cavity of the processus vaginalis and the peritoneal cavity is usually closed before birth. The cavity of the part of the processus that extends from the deep ring to the scrotum is usually obliterated during the first month after birth, and its wall becomes a fibrous thread (the vestige of the processus vaginalis). The part of the processus that reaches the scrotum persists as the tunica vaginalis testis. The cavity of tunica vaginalis is now entirely separated from the peritoneal cavity, but its wall is still connected with the peritoneum for a longer or shorter time, by the vestige of the processus. However, the vestige undergoes atrophy from below upwards and frequently, as already mentioned, it entirely disappears.

2. The factors responsible for, testicular descent.

The exact cause of descent of testis and processus vaginalis is still a subject of dispute. However, the following factors contribute to the descent of testis:-

2.1. Gubernaculum testis; - This is considered to be the most important musculo-fibrous structure and factor, which brings and guide testis to the scrotum. Failure of its proper mechanism gives rise to cryptorchism and ectopic testis. [20]

2.2. Intra abdominal pressure; - tends to displace the testis downwards. In undescended testis, continuous intra abdominal pressure causes atrophy of testis, and they are more prone to developing malignancies.

2.3. The differential growth of abdominal wall.

2.4. Intra abdominal temperature; - the temperature in the abdomen is two degrees more than the scrotum. If the testis remains inside the abdomen (as in undescended testis), it hurts spermatogenesis.

2.5. Calcitonin gene related peptide (CGRP);- It is a neurotransmitter secreted by the genitofemoral nerve, supplying the muscular fibres of gubernaculum testis.

2.6. Male sex hormones-In the male Y chromosome has a gene for testis determining factor (TDF). Under the influence of TDF, the development of gonads proceeds in the male direction and testis develops, while in a female in the absence of TDF the development of gonads proceed in female guidance and ovaries develop.

2.7. Sexual development begins at the approximately 8th week of gestation with the production of Mullerian-inhibiting substance/anti-Mullerian hormone (MIS/AMH). It triggers Mullerian duct regression along with testosterone, stimulating the Wolffian duct to persist and to form, the epididymis, vas deference and seminal vesicles. [21-22] Mullerian inhibiting substance (MIS/AMH) is a glycoprotein dimer (mw 140,000) produced by the Sertoli cells. It is also secreted in the Wolffian duct and then diffuses laterally into the adjacent Mullerian duct to trigger its regression in the male. It may also have some secondary role in the development of gubernaculum and has post natal functions in the ovarian cycle. [23]

2.8. Insulin like hormone 3 (INSL 3): - It is a protein with homology to the insulin that is produced by the Leydig cells. It stimulates the growth of the gubernaculum, which is important for the first phase of the testicular descent. [24]

2.9. Calcitonin gene related peptide (CGRP); - it is a neurotransmitter secreted by the genitofemoral nerve, supplying the muscular fibres of gubernaculum testis. It provides a chemotactic gradient for the gubernaculum to follow. [25]

2.10. Maternal gonadotrophins; - However the gubernaculum testis is considered an important factor for the formation of processus vaginalis and in guiding testis to the scrotum. The descent is also required for the propagation of the species since intra abdominal pressure and temperature has an inhibitory effect on spermatogenesis.

Thus we see that the testicular descent is a complex and multifactorial event, and cryptorchism should be viewed as a disease with multiple aetiologies.

3. Why the ovaries do not descent to labia? (In Females)

The initial phase of descent of ovaries is similar to that of the testis. There is the formation of gubernaculum of ovaries; there is also the formation of the inguinal canal and processus vaginalis. In females, the gubernaculum is attached to developing uterus close to fallopian tubes so it may be seen as two parts of gubernaculum.

1). The first part extends from the lower pole of the ovary to the uterus. This part forms the ligament of the ovary.

2). The other part extends from uterus to labia majora. This part passes through inguinal canal and forms round ligament of the uterus.

The first part of descent of ovary up to the pelvic brim takes place because of the growth of posterior abdominal wall and pelvis.

Ovaries are prevented from entering the inguinal canal because of the attachment of gubernaculum to the uterus when uterus descends into the pelvic cavity the ovaries are also carried along with it. Since the ovaries do not traverse the inguinal canal, the processus vaginalis and inguinal canal remain small and rudimentary.

4. The pathology related to descent of testis

The descent of testis may become erratic and gives rise to following pathological conditions:-

4.1. Related to gubernaculum testis:-

1). Undescended testis.

2). Ectopic testis.

4.2 Related to processus vaginalis:-

1). Congenital hernia.

2). Congenital hydrocoel.

4.1.1. Undescended testis

The descent of testis may be arrested at any point in its journey, from lumbar region to scrotum, depending upon the arrest of descending and its abnormal location. [26-28]

The undescended testis may be found at:-

a. Lumbar region -due to total failure of descending,

b. Iliac region – where in the testis are situated at the entry of inguinal canal, near deep inguinal ring (seven-month position).

c. Inguinal-situated within the inguinal canal.

d. Pubic- located at the superficial inguinal ring.

e. Scrotal- located high up in scrotum.

4.1.2. Ectopic testis

In this condition, the testis frequently descends, from the posterior abdominal wall, negotiate through the deep inguinal ring to the inguinal canal and comes out through superficial inguinal ring. However, it fails to reach to the scrotum. It deviates from its path of normal descend. It is thought to be due to many tails of gubernaculum. There is a failure of primary gubernaculum functioning and activation of one of its "tail", which pulls the testis to an unusual position. Thus ectopic testis may be found at abdominal, pubo-penile, femoral, perineal, or contra lateral scrotal positions.

4.2. Congenital hydrocele/hernia

The processus vaginalis is a diverticulum of the abdominal peritoneum. It obliterates once the descent of testis is over. If it is not obliterated as happens, then it may give rise to following pathological conditions:-

a. Congenital hydrocele: - It is a persistent congenital sac of the peritoneum, with a tiny communication between processus vaginalis and peritoneal cavity. It may contain fluid and thus presents as congenital hydrocele.

b. Hydrocoel of cord: - The processus is obliterated at above and below having a cystic space shut off from peritoneal cavity above and cavity of tunica below. This is called the encysted hydrocele of cord.

c. A congenital hernia: -The processus vaginalis fails to obliterate, and the communication to peritoneal cavity is sufficiently significant to permit passage of abdominal content into the sac. This condition is called congenital inguinal hernia.

5. What this paper contributes/Highlights

- It highlights the mechanism of testicular descent to the scrotum, which is essential for proper spermatogenesis and propagation of species.
- It explains why the blood supply of testis and epididymis comes all the way from the abdomen.
- It describes the mechanism and probable causation of ectopic and undescended testis.
- It also highlights the factors responsible for a congenital hernia and hydrocele.

Authors' Statements

Competing Interests

The authors declare no conflict of interest.

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