TESTES DEVELOPMENT AND DESCENT AND CLINICAL ENTITIES DURING DESCENT

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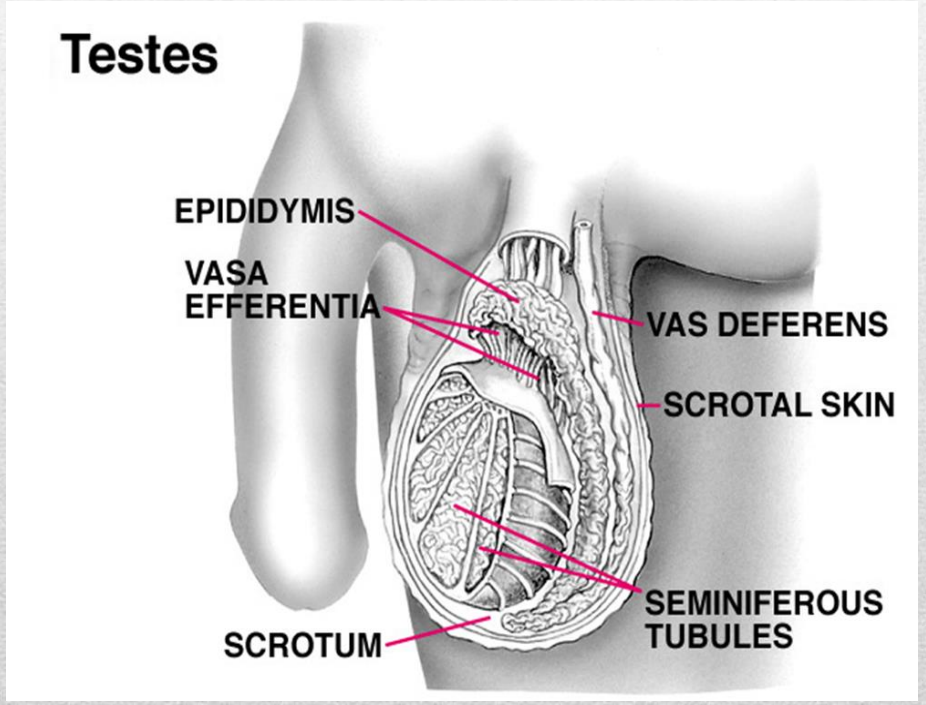
Overview

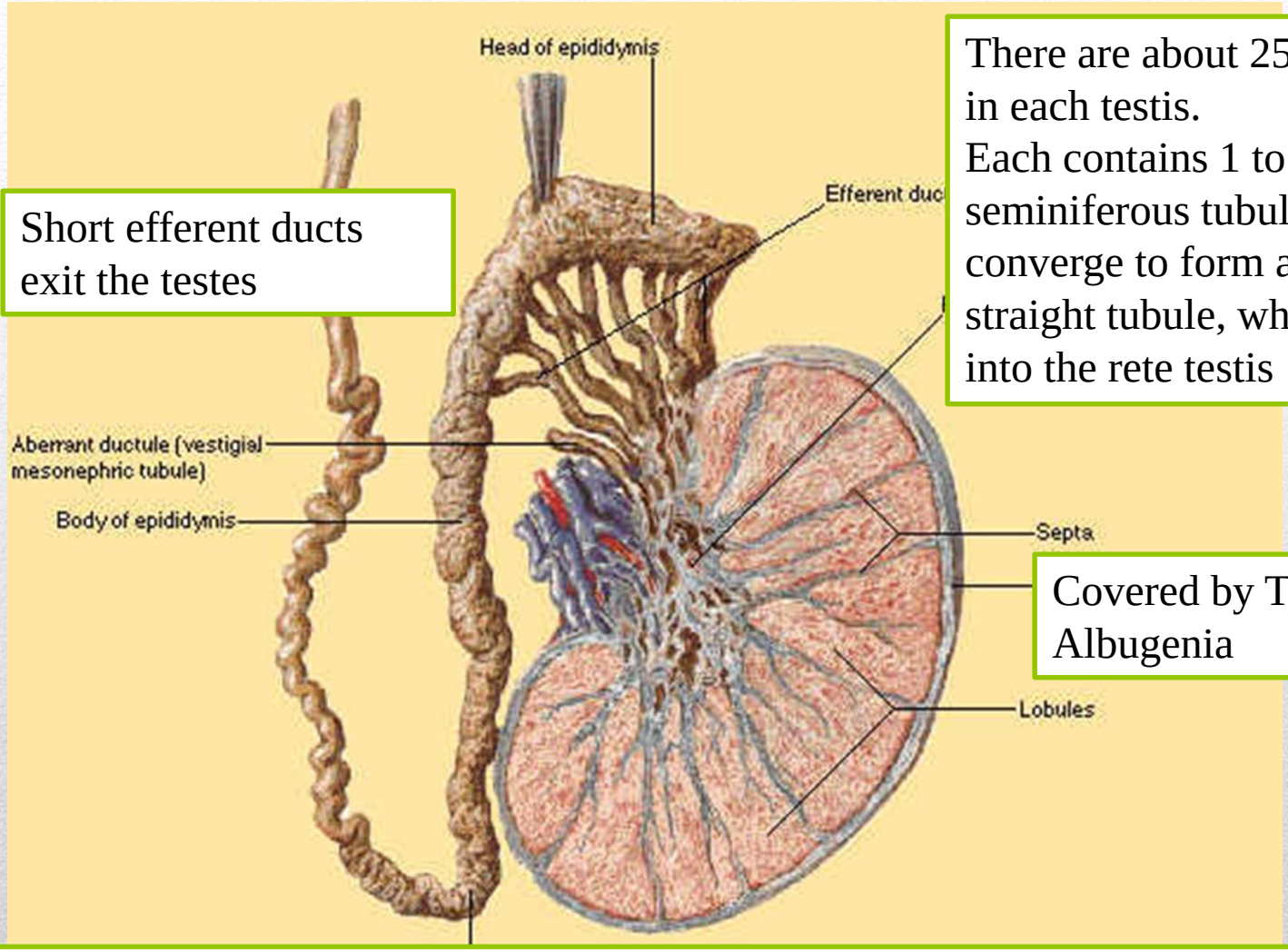
- Anatomy of Testes
- Development of Testes
- Descent of Testes
- Anomalies of Descent of Testes

Anatomy of Testes

Testes

- Each testis is an oval structure about 5 cm long and 3 cm in diameter
- Suspended by: spermatic cord
- Located in the scrotum





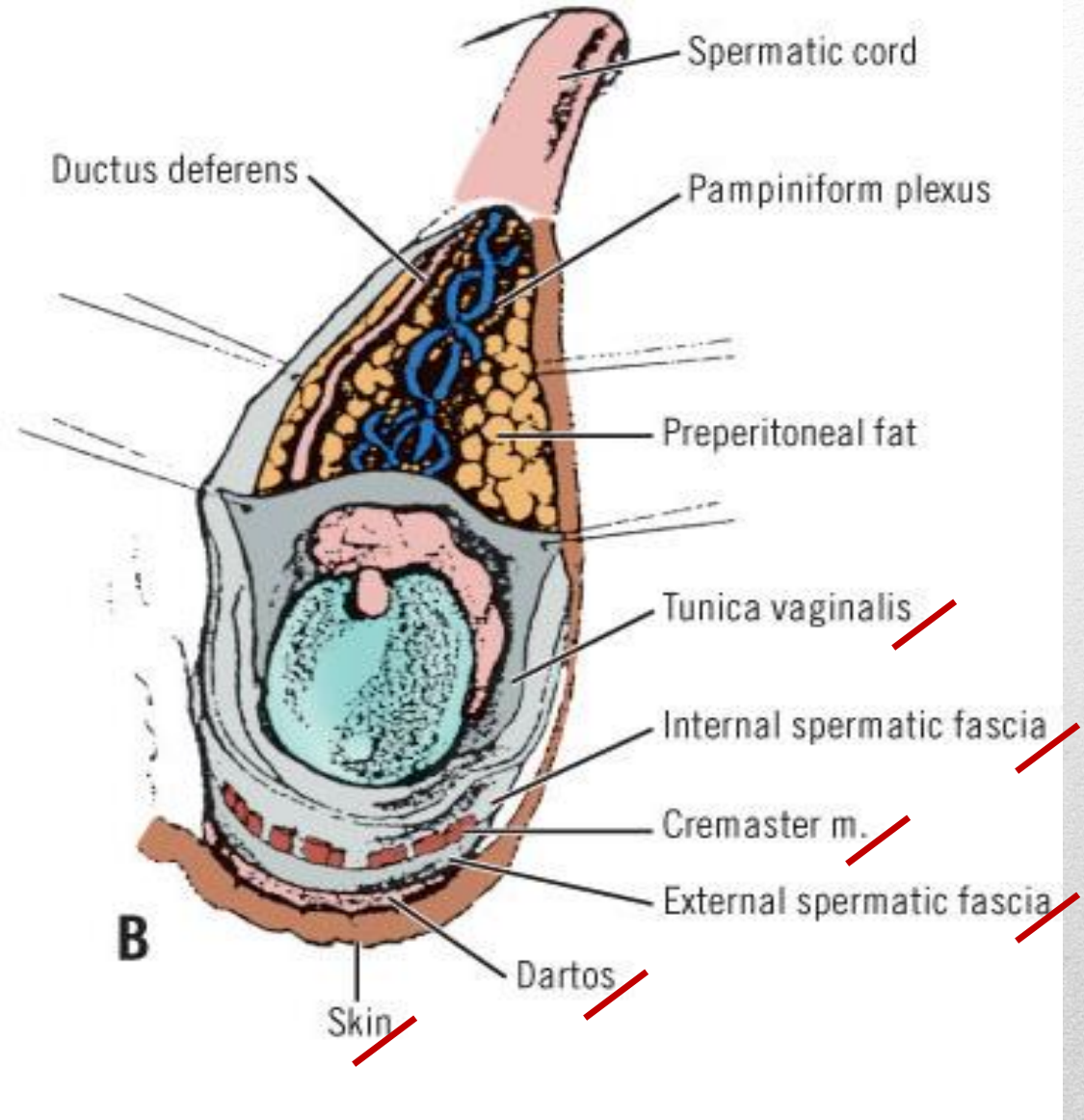
Short efferent ducts exit the testes

There are about 250 lobules in each testis.
Each contains 1 to 4 - seminiferous tubules that converge to form a single straight tubule, which leads into the rete testis

Covered by Tunica Albugenia

Interstitial cells (cells of Leydig), which produce male sex hormones, are located between the seminiferous tubules within a lobule

Coverings of the Testes



Gonadal Genesis

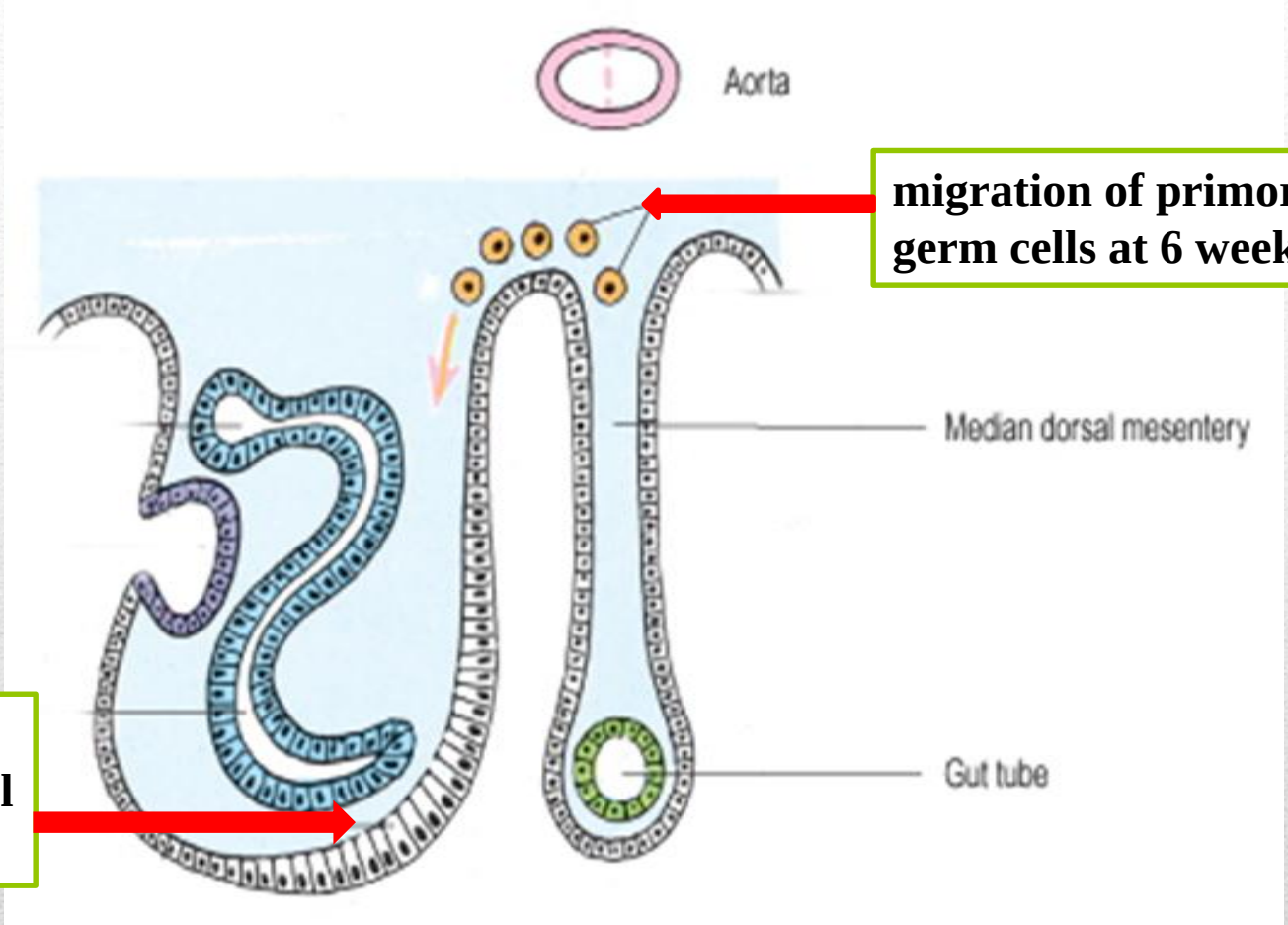
- The gonads develop near the kidney in the retroperitoneal space at the lumbar area

- Formation of the gonad is dependent upon three primordia:

  Primordial germ cells

  Genital ridge. The genital ridge is formed by the mesenchyme of the ventromedial aspects of the mesonephros close to the root of the mesentery

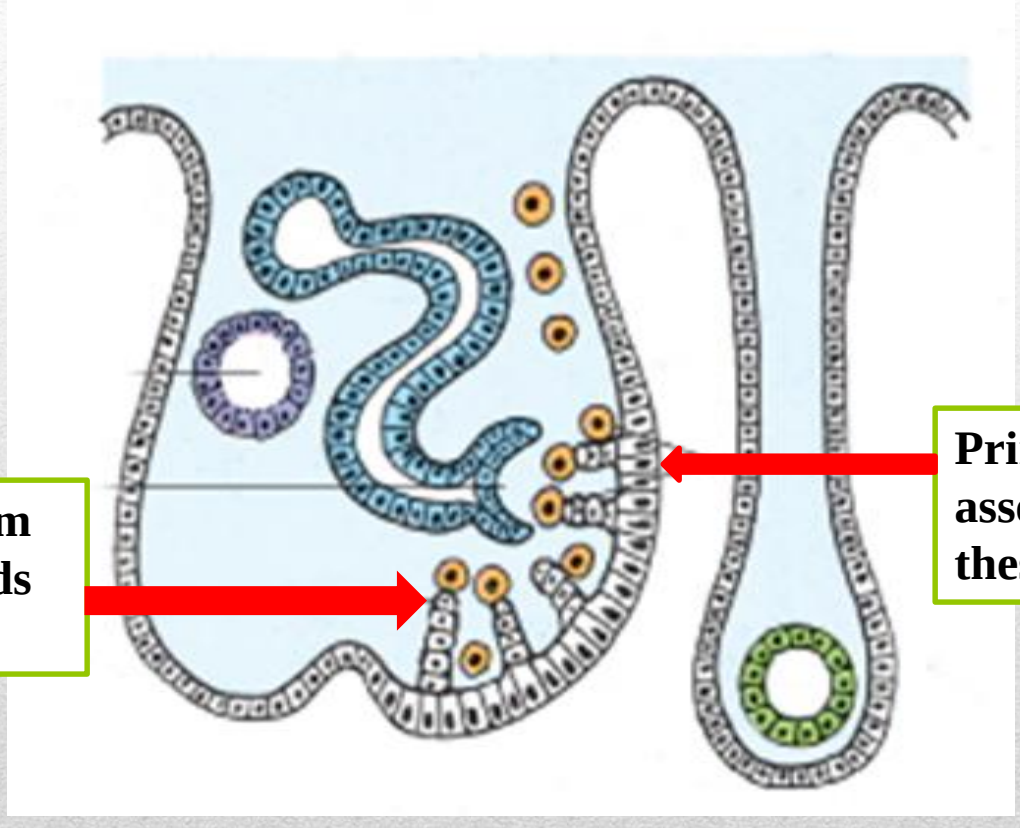
  Coelomic epithelium overlying the mesenchyme



migration of primordial germ cells at 6 weeks

At 4 to 6 weeks of gestation, the genital ridges organize

At the end of the seventh week or early in the eighth week, the differentiation stage **initiated by the *SRY* gene**



The coelomic epithelium develops epithelial cords (germinal cords)

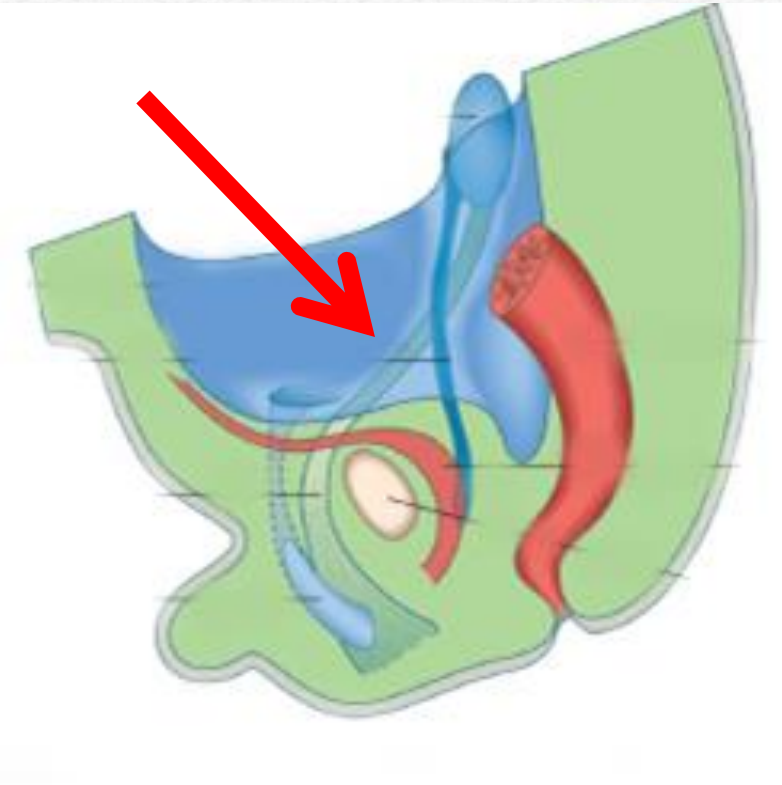
Primodal sex cells associate with these sex cords

- During this period the testes are suspended by the mesorchium, a double peritoneal fold
- The lower fold forms the ***hunterian gubernaculum***
- The upper fold transmits the spermatic vessels
- Gubernaculum appears at the 7th week of embryologic development as a condensation of mesenchymal tissue within the subserous fascia on either side of the vertebral column

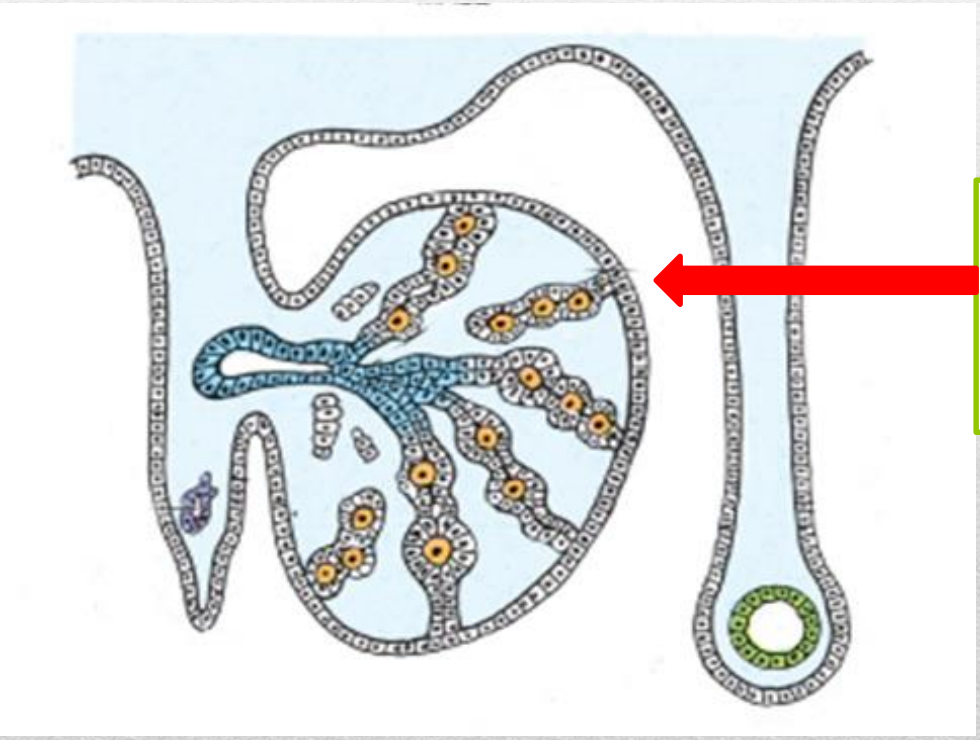
- The cranial aspect of the gubernaculum envelops the cauda epididymis and lower pole tunica albuginea of the testis and extends caudally into the inguinal canal, where it maintains a firm attachment

- The gubernaculum is not firmly attached to the scrotum but is in continuity with the scrotum by the mesenchymatous tissue that fills the scrotum

- Just before testicular descent, the gubernaculum undergoes a significant increase in length and rapid enlargement in gubernacular mass

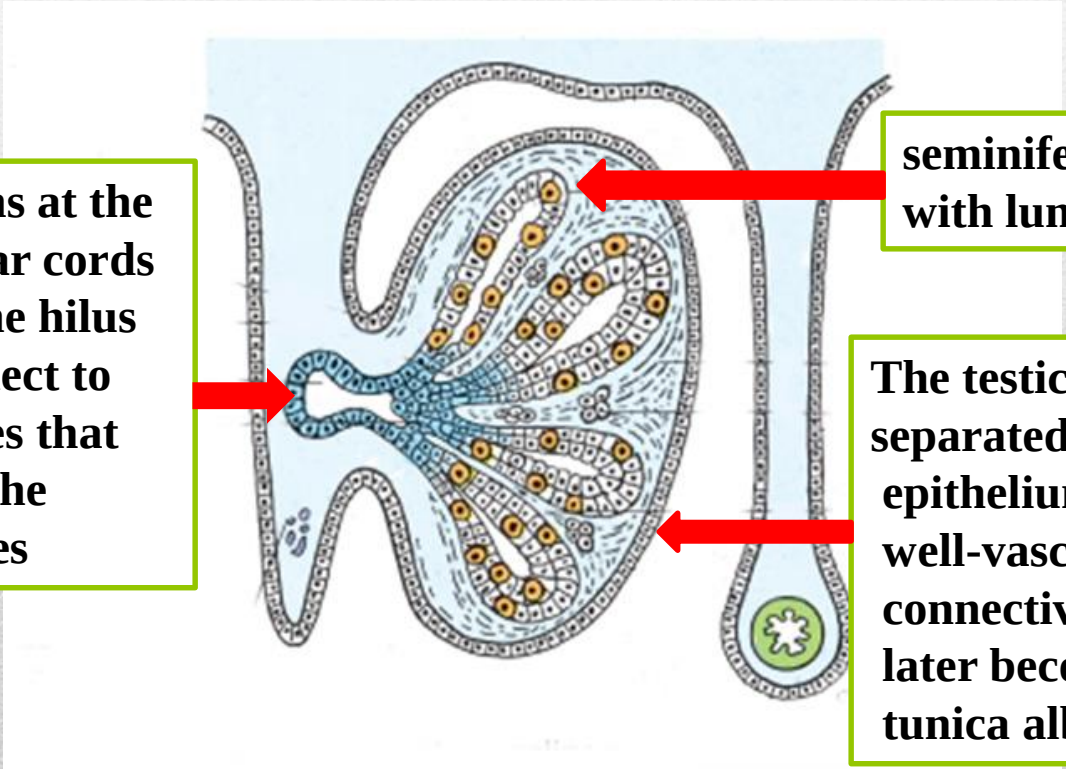


- **By 7 weeks, primitive Sertoli cells have developed**
- **Germ cells differentiate into gonocytes on entering the testicular cords to become fetal spermatogonia by 15 weeks of gestation**



Gonocytes and Sertoli cells form testicular cords within the testis and canalize to form seminiferous tubules

- **By the eighth week of gestation, Leydig cells have differentiated around the testicular cords in the gonadal mesenchyme between the seminiferous tubules**



The rete testis forms at the ends of the testicular cords and converges at the hilus of the testis to connect to the efferent ductules that differentiate from the mesonephric tubules

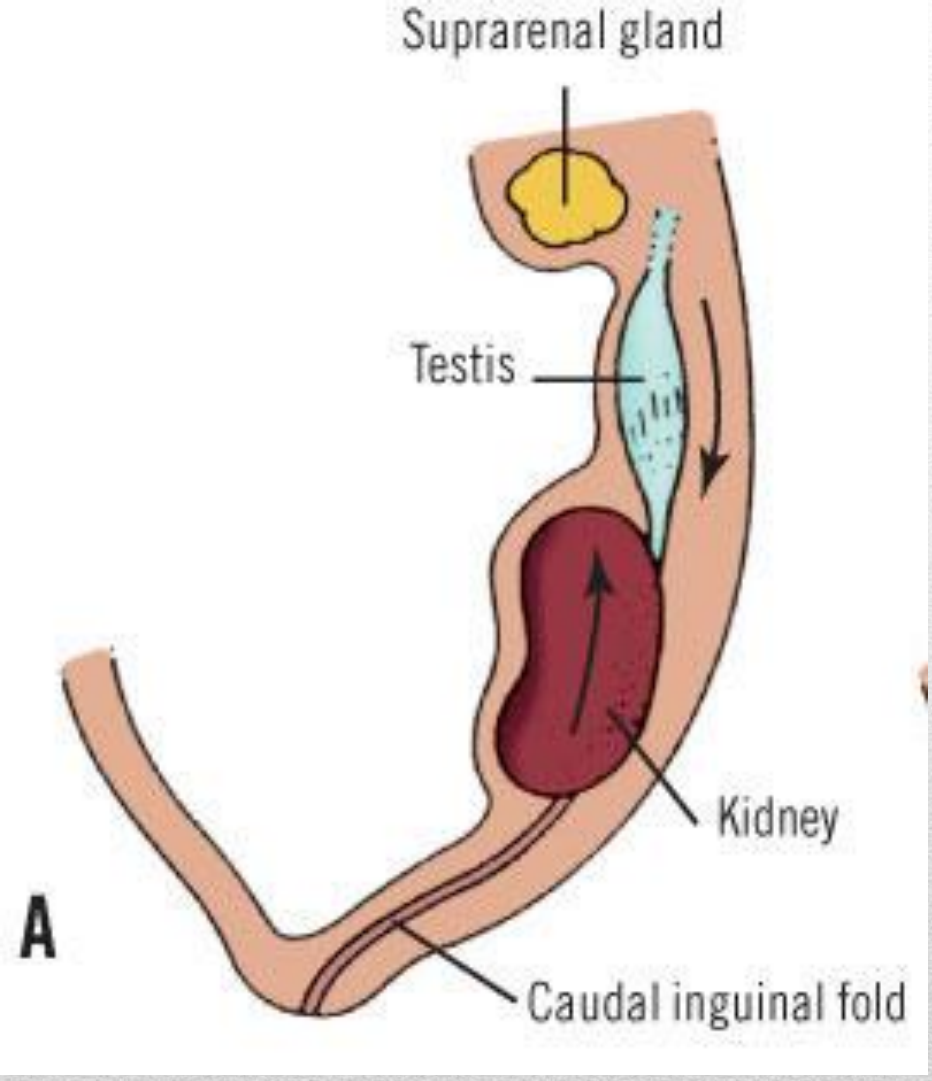
seminiferous tubules with lumen

The testicular cords separated from the coelomic epithelium by a well-vascularized connective tissue layer that later becomes the tunica albuginea

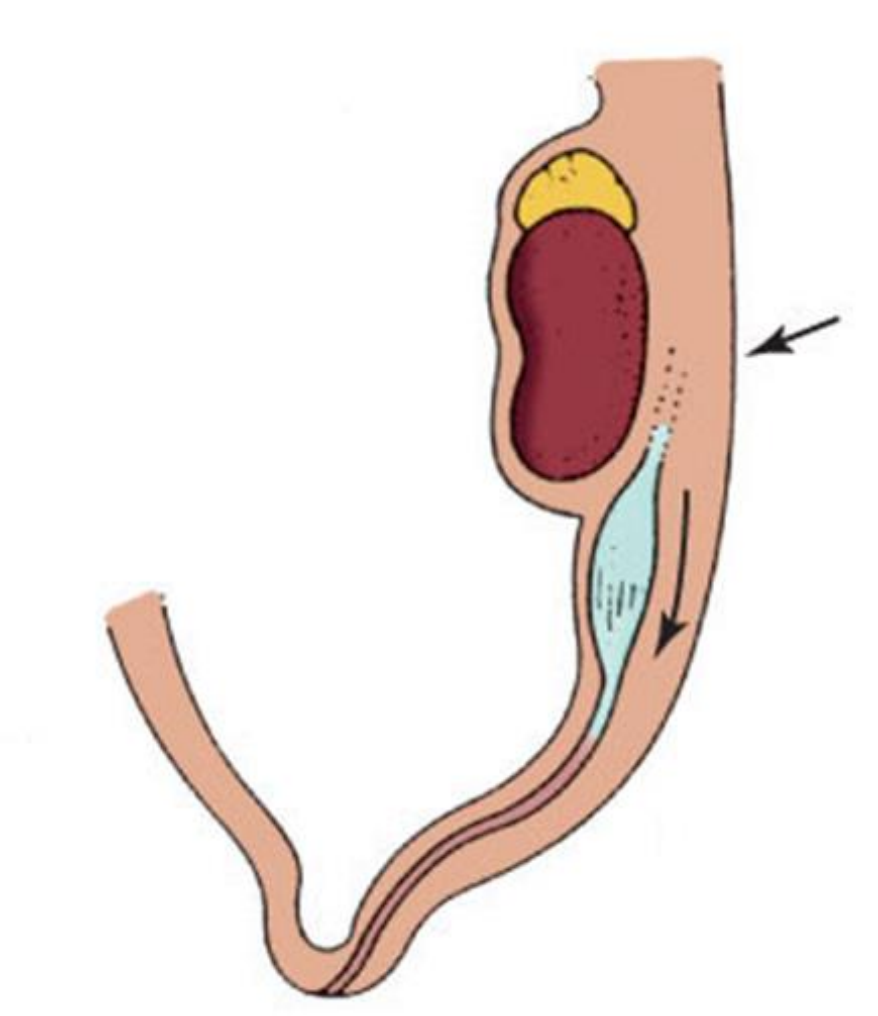
Descent of the testis

- The testis that has not begun its descent together with the epididymis is attached to the posterior abdominal wall by a mesorchium
- It may lie at the level of the upper pole or the lower pole of the kidney, the iliac fossa, or in the pelvis
- The downward journey commences at approximately the 3rd month of gestation
- The pathway is retroperitoneal

- 5th week
- Testis begins its primary descent; kidney ascends



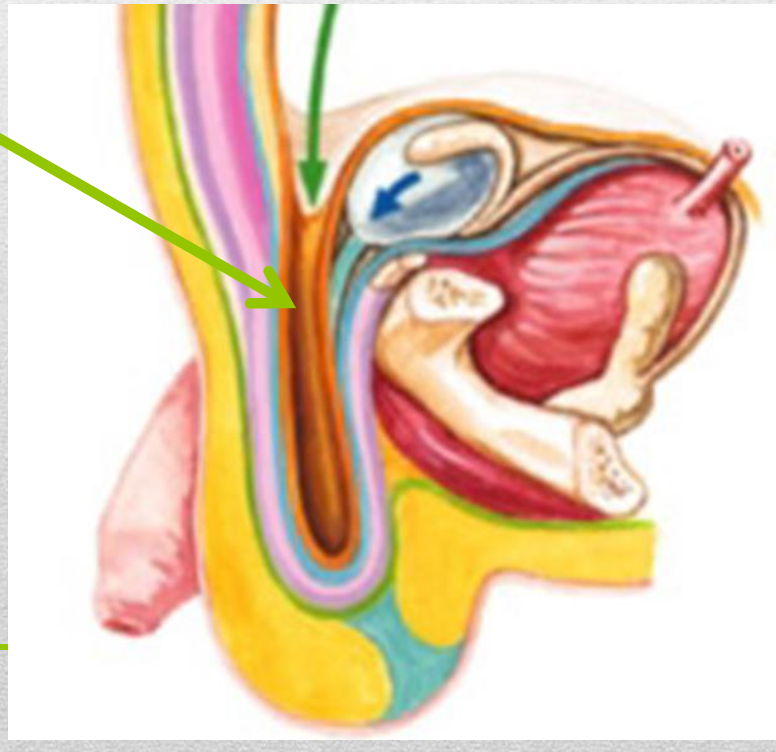
- 8th to 9th weeks
- Kidney reaches adult position



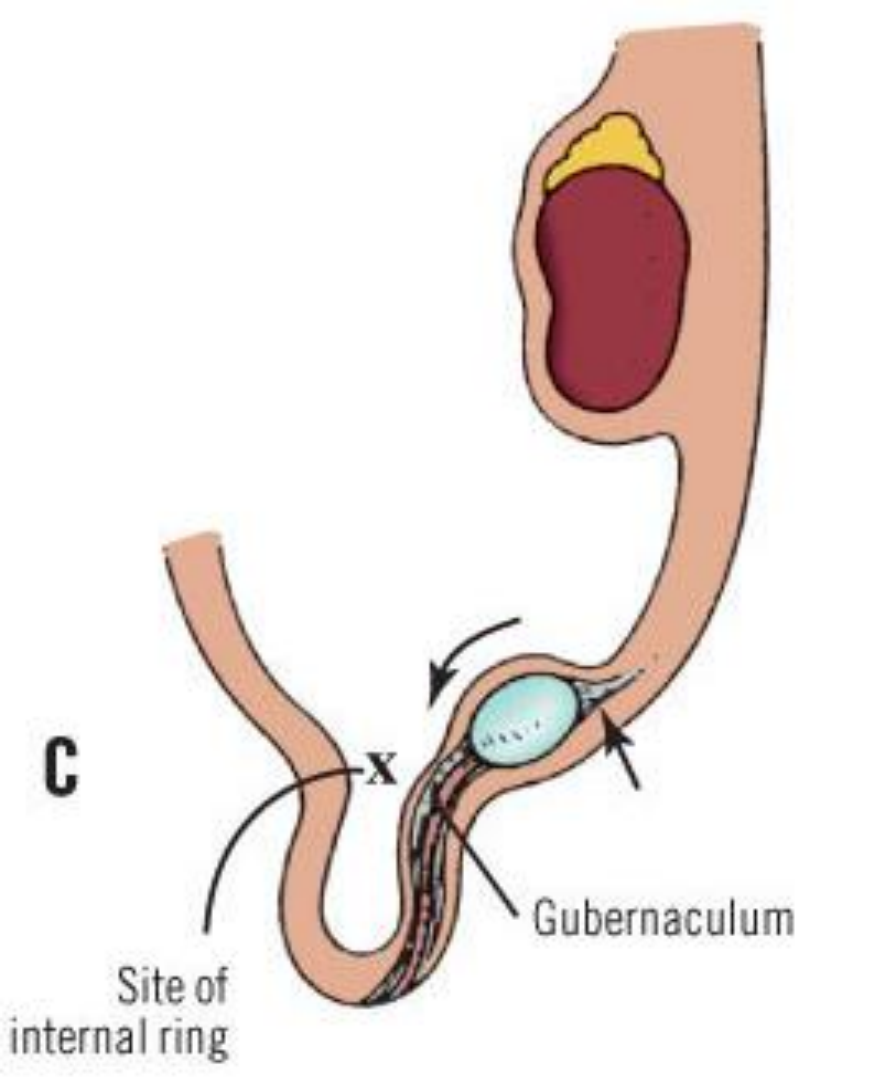
- During the 7th month the testes are found at the level of the anterior superior iliac spine

- The peritoneum dips into the inguinal canal ahead of the testes, but extends down the gubernaculum only part way, known as ***Processus Vaginalis***

- The testes and gubernaculum extend into the canal

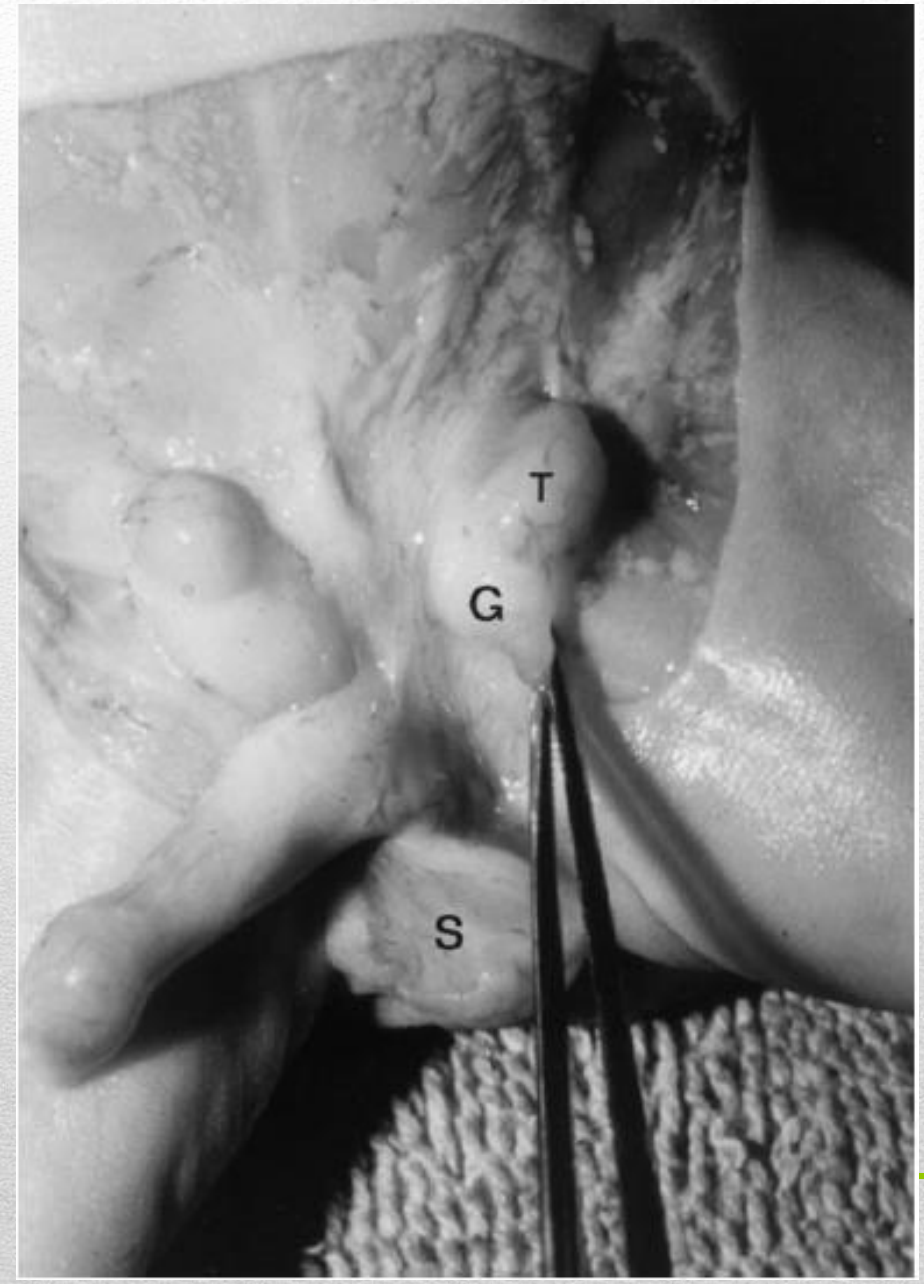


- The testes begin to enter the internal ring as the gubernaculum emerges from the external ring
- At about the end of the 7th month, the testes pass through the inguinal canal



- The bulbous lower end of the gubernaculum loses its firm attachments to the inguinal canal after the testis descends through the canal

- The gubernaculum has an important role in fixation of the testis to the inguinal canal before descent, but its role in descent of the testis through the canal and into the scrotum is less obvious



- Dissection of 32-week human fetus showing
- the testis (T) and gubernaculum (G) migrating across the pubic region toward the scrotum(S)
- A pair of forceps holds the caudal end of the gubernaculum

- Although descent through the canal is accomplished in a few days, it takes four additional weeks for the testes to pass from the external ring to the bottom of the scrotum

- **Testicular descent occurs in**

  80% at 34 weeks of gestation

  75% at 28 weeks of gestation

  50% at 27 weeks of gestation

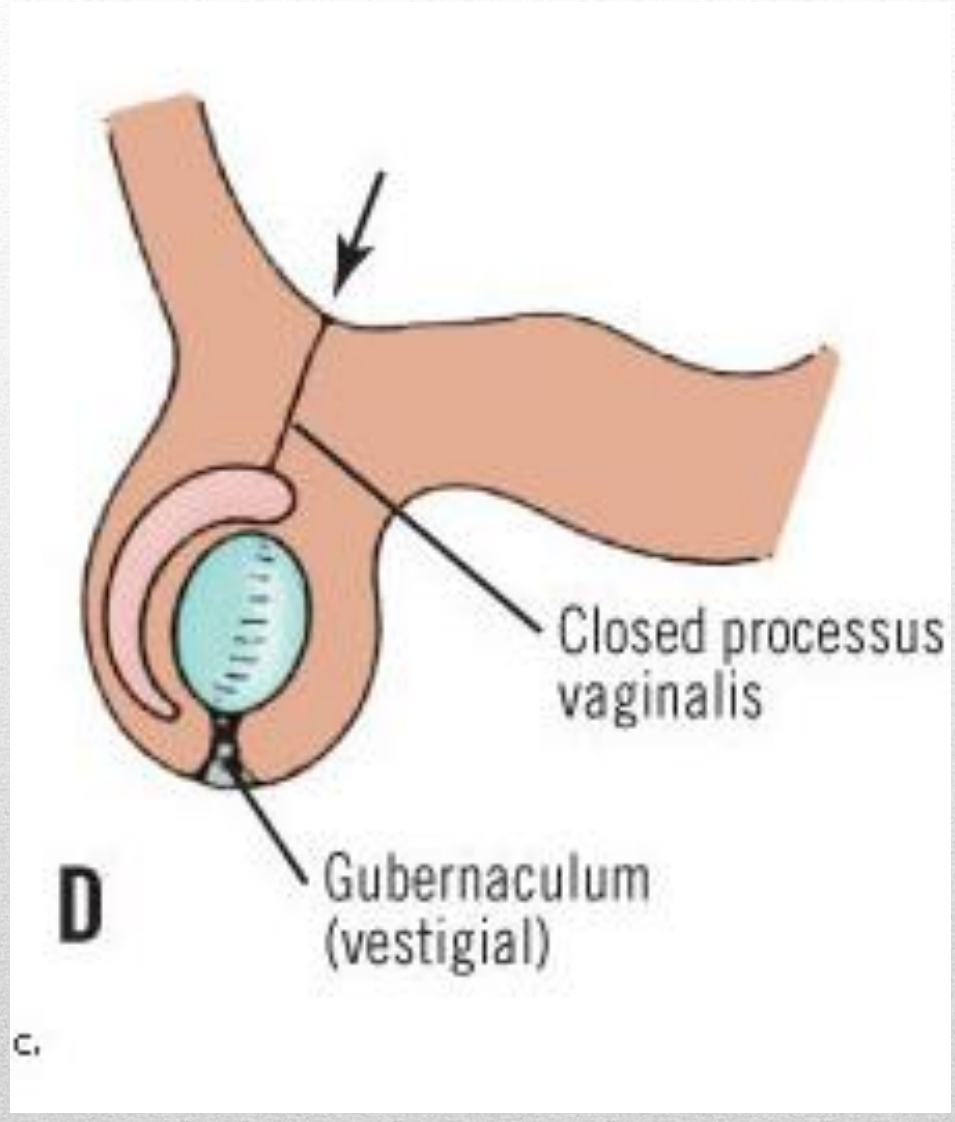
  10% at 24 weeks of gestation

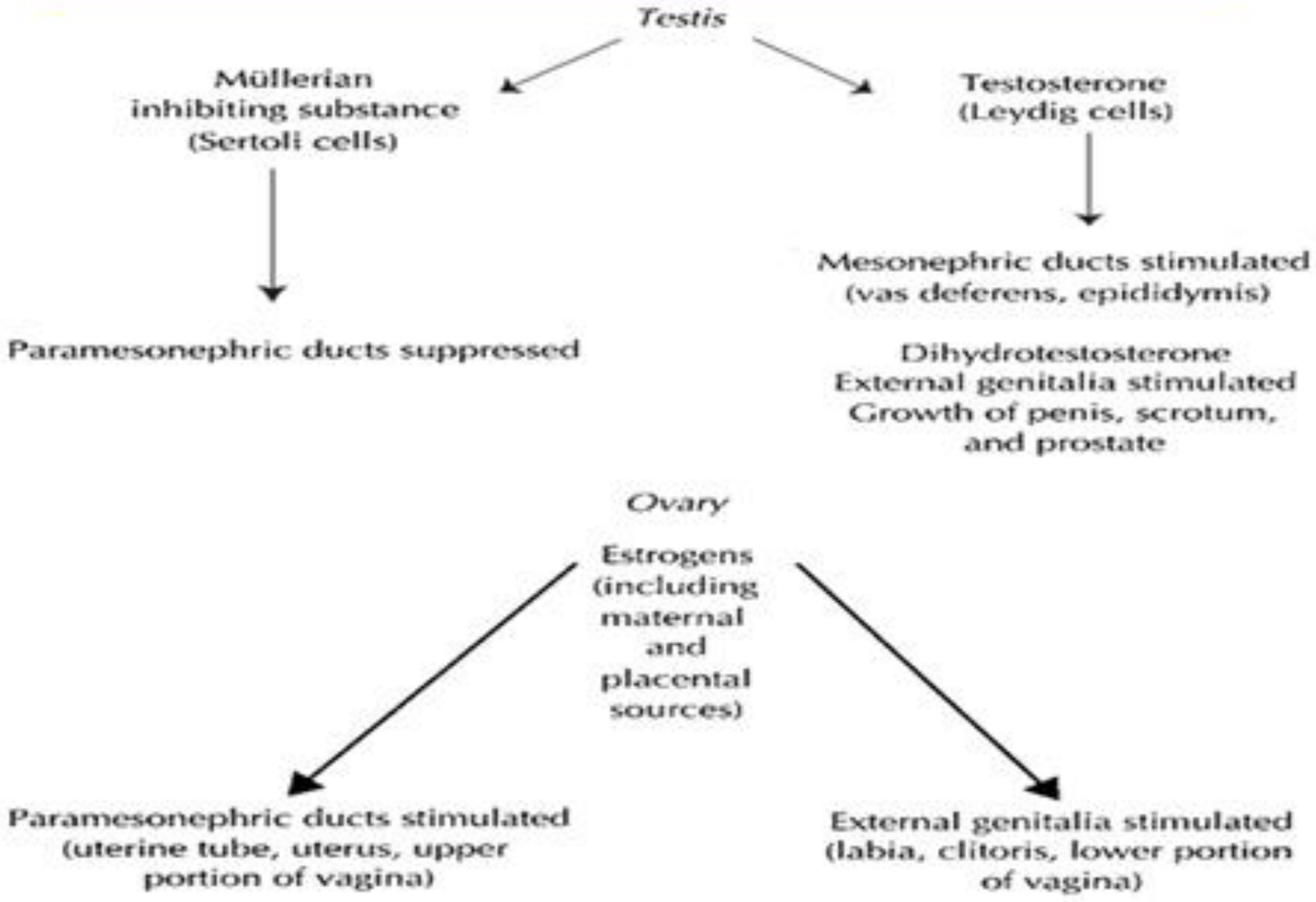
- the left testis usually migrates ahead of the right

- Postnatal life

- Testis in scrotum
- processus vaginalis closed
- gubernaculum (vestigial)

  scrotal ligament of Lockwood




Testis
Müllerian inhibiting substance (Sertoli cells)
Testosterone (Leydig cells)
Paramesonephric ducts suppressed
Mesonephric ducts stimulated (vas deferens, epididymis)
Dihydrotestosterone
External genitalia stimulated
Growth of penis, scrotum, and prostate
Ovary
Estrogens (including maternal and placental sources)
Paramesonephric ducts stimulated (uterine tube, uterus, upper portion of vagina)
External genitalia stimulated (labia, clitoris, lower portion of vagina)

Factors influencing the Descent

Factors affecting Descent

Endocrine

1. HPG Axis
2. Androgens
3. MIS
4. Estrogen
5. Descendin

Anatomical

1. Gubernaculum
2. Genitofemoral N & CGRP
3. Abdominal Pressure

Hypothalamic-Pituitary-Gonadal Axis

- A normal hypothalamic-pituitary-gonadal axis is usually a prerequisite for testicular descent to occur
- The primary hormones that regulate the testes are luteinizing hormone (LH) and follicle stimulating hormone (FSH)
- Plasma FSH levels are often elevated in patients with testicular pathology, including those with cryptorchidism

Androgens

- The androgens - testosterone and DHT are necessary for testicular descent to occur
- They may act either directly or indirectly, such as in the neuroendocrine modulation of the GFN and release of calcitonin gene–related peptide (CGRP)
- Androgens do not mediate the first phase of testicular descent

- However, androgens appear to be important for the inguinal-scrotal phase of testicular descent.
- Failure of gubernacular involution has been observed in humans with AIS.. Hutson and Donahoe, 1986
- Clinical examples supporting this theory - androgen insensitivity syndrome (AIS) and hypogonadotropic hypogonadism who have bilateral cryptorchidism

Müllerian Inhibiting Substance

- MIS is secreted by the fetal Sertoli cells and is responsible for regression of the müllerian ducts
- Also being implicated in effecting testicular descent
- MIS does not play a significant role in the regulation of testicular descent

- (1) normal testicular descent occurs in MIS-deficient knockout Mice...Behringer et al, 1994
- (2) normal testicular descent occurs in fetal rabbits immunized with bovine MIS....Tran et al, 1986
- (3) the majority of patients with intra-abdominal testes do not have retained müllerian derivatives.

Estrogen

- Estrogens have been postulated to impair testicular descent
- Prenatal treatment with diethylstilbestrol (DES) ...a nonsteroidal synthetic estrogen, is associated with urogenital abnormalities in both male and female fetuses. Undescended testes is one of the abnormalities observed in 46,XY fetuses.....Stillman, 1982
- Estrogens are thought to impair gubernacular development and to cause persistence of müllerian duct derivatives
- Animal studies on mice confirmed that prenatal estrogen exposure disrupts the transabdominal phase of testicular descent…McLachlan et al, 1975 ; Shono et al, 1994

Descendin

- Descendin, a gubernacular-specific growth factor
- Direct stimulation of the human gubernaculum via specific intranuclear hormone receptor binding, thus implicating its role in gubernacular swelling through an increase in glycosaminoglycans

Gubernaculum

- All evidence implicates the gubernaculum as the major factor responsible for testicular descent
- Earliest theories were based on preconceived notions of testicular descent and suggested that the testis was pulled into the scrotum by the gubernaculum
- However, substantial evidence indicates that there is no firm attachment of the gubernaculum to the scrotum...Wensing, 1968 ; Scorer and Farrington, 1971 ; Heyns,1987 ; Wensing, 1988 ; Hutson et al, 1997

Genitofemoral Nerve and Calcitonin Gene–Related Peptide

- Lewis first presented evidence in 1948 that transecting the GFN in neonatal rats resulted in cryptorchidism

- Transection of the GFN in rats resulted in the testes remaining in the abdomen and prevented gubernacular migration..Beasley and Hutson, 1987 ; Fallat et al, 1992

- The concept that the GFN acts as a “second messenger” is based on evidence that androgens increase the number of GFN cell bodies and promote gubernacular migration, mediated by CGRP..Hutson and Beasley, 1987

- CGRP has been identified as a neurotransmitter in the GFN and its nerve branches

Intra-abdominal Pressure

- Abdominal pressure probably has an ancillary role in migration of the testis from the abdominal cavity to the inguinal canal, but thereafter it plays a more significant role in ***transinguinal descent*** into the scrotum

- The patent processus vaginalis works in conjunction with intra-abdominal pressure, which is transmitted to the testis during transinguinal migration.

- Conditions that result in cryptorchidism hypothetically associated with decreased intra-abdominal pressure include :

1. prune-belly syndrome
2. cloacal exstrophy
3. Omphalocele
4. gastroschisis,
5. a number of syndromes characterized by both cryptorchidism and congenital abdominal wall muscular defects or agenesis

...Levard and Laberge, 1997 ; Koivusalo et al, 1998

Abnormalities of Testicular Descent

- **Cryptorchidism:** testis neither resides nor can be manipulated into the scrotum
- **Ectopic**: aberrant course
- **Retractile**: can be manipulated into scrotum where it remains without tension
- **Gliding**: can be manipulated into upper scrotum but retracts when released
- **Ascended**: previously descended, then “ascends” spontaneously

Cryptorchidism

Percentages of testes arrested at different stages of normal descent

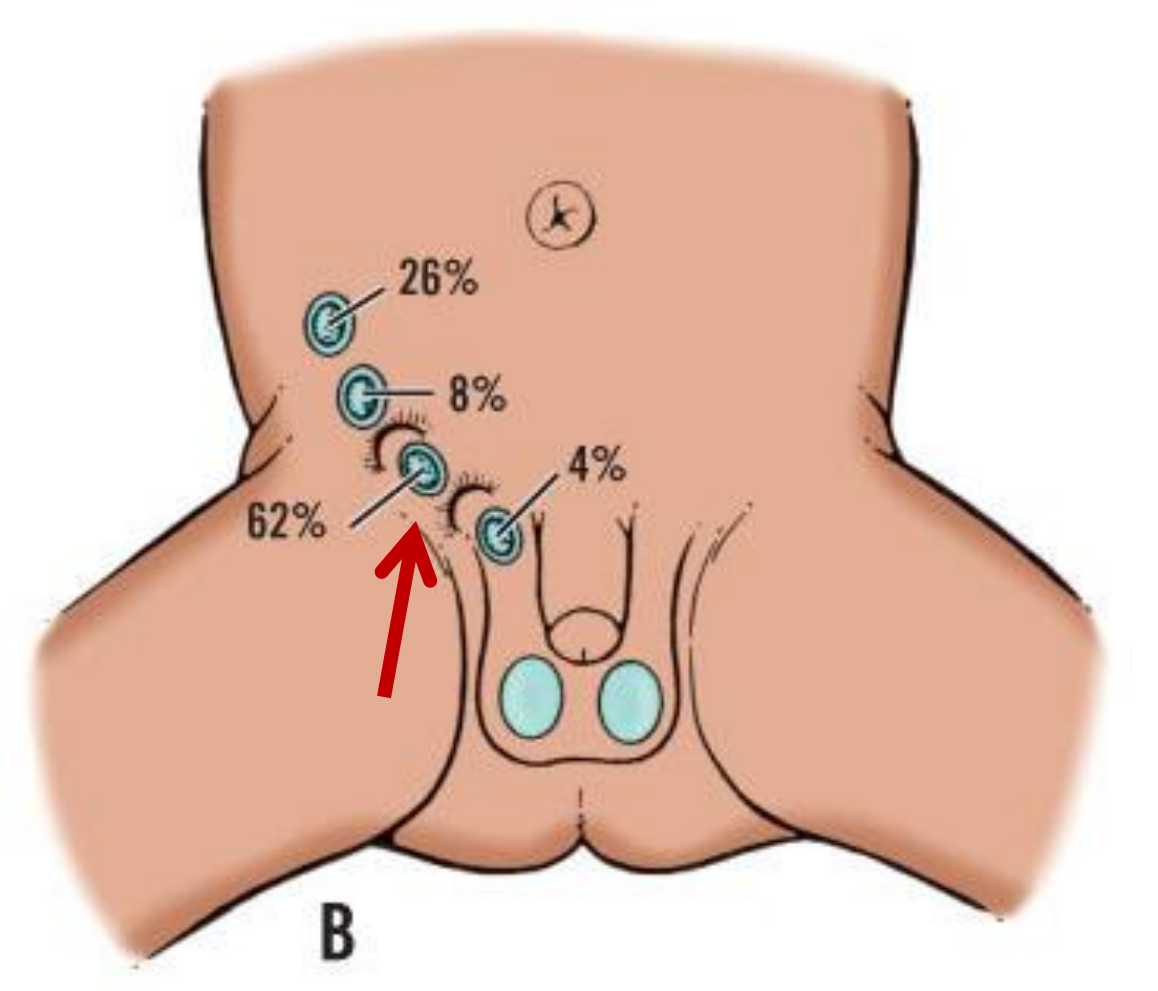
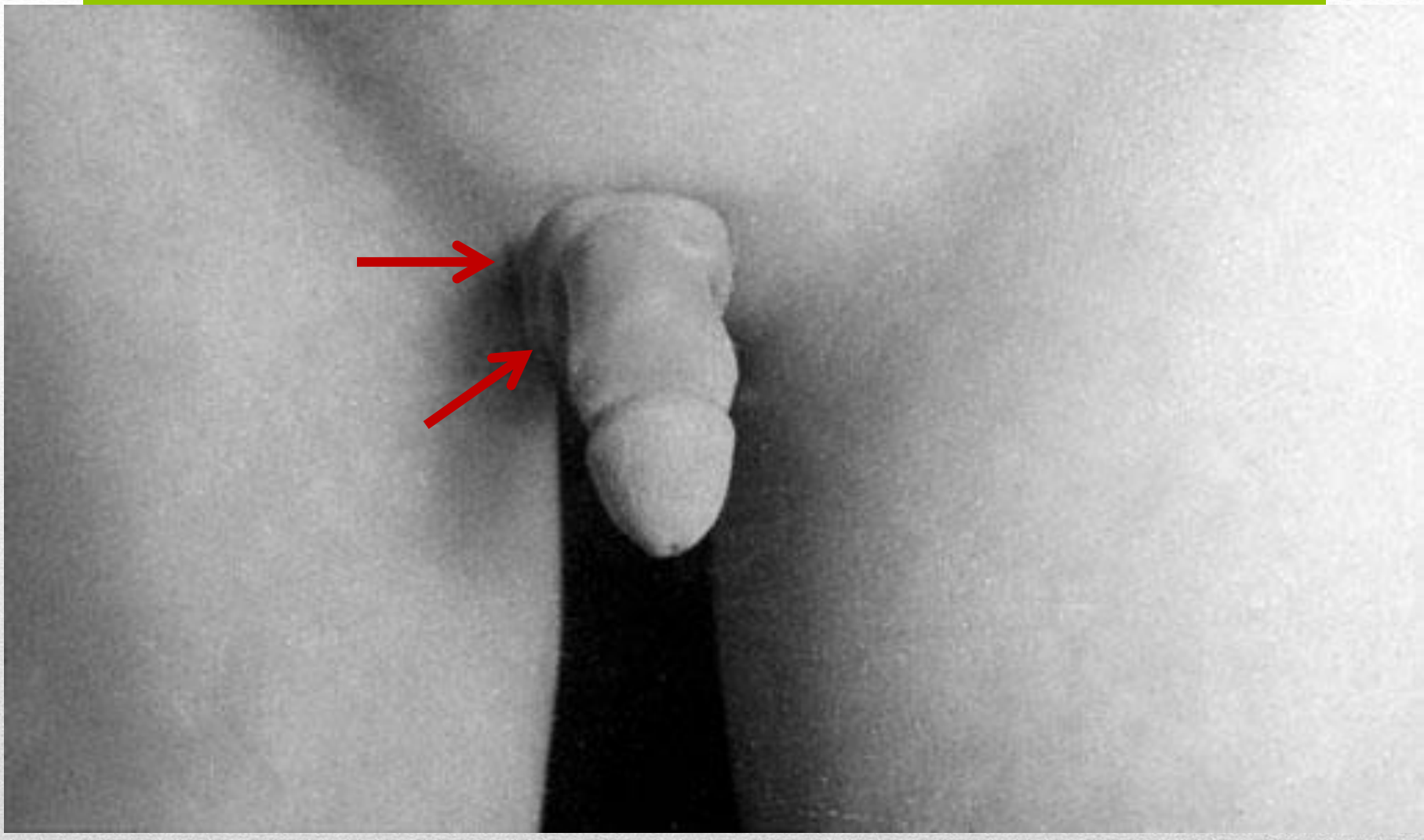
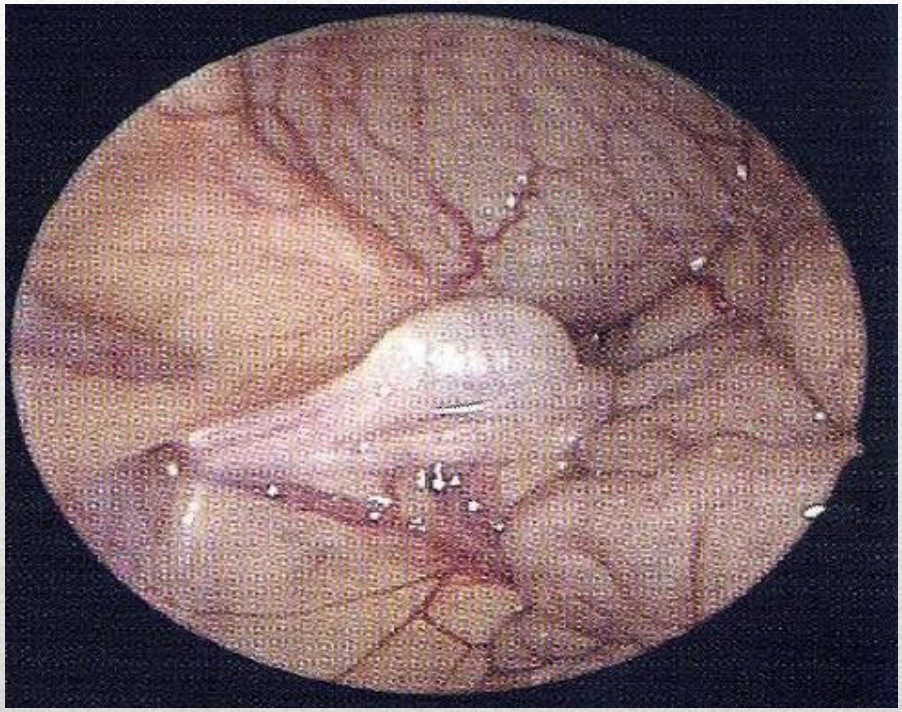


TABLE 3. Possible causes of cryptorchidism

A. Androgen deficiency/blockade
   Pituitary/placental gonadotropin deficiency
   Gonadal dysgenesis
   Androgen synthesis defects (rare)
   Androgen receptor defects (rare)
B. Mechanical anomalies
   Prune belly syndrome (bladder blocks inguinal canal)
   Posterior urethral valves (bladder blocks inguinal canal)
   Abdominal wall defects (low abdominal pressure/gubernacular rupture)
   Chromosomal/malformation syndromes (? connective tissue defects block migration)
C. Neurological anomalies
   Myelomeningocele (GFN dysplasia)
   GFN/CGRP anomalies
D. Acquired (?) anomalies
   Cerebral palsy (cremaster spasticity)
   Ascending/retractile testes (? fibrous remnant of processus vaginalis)



A cryptorchid in a boy aged 12 years. Note the retracted underdeveloped scrotum.



Intra-abdominal testis

Consequences of Cryptorchidism

- Infertility
- Neoplasia
- Congenital Hernia
- Testicular Torsion

Neoplasia

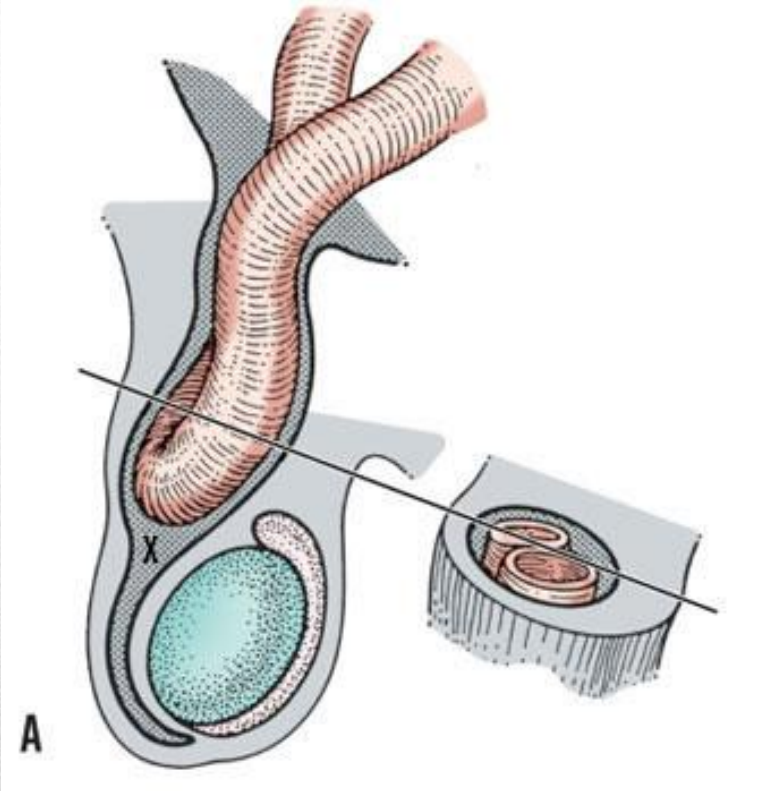
- Approximately 10% of testicular tumors arise from an undescended testis...Whitaker, 1970 ; Abratt et al, 1992
- The incidence of a testicular tumor in the general population is 1 in 100,000, and the incidence of a germ cell tumor in men formally cryptorchid is 1 in 2550
- The relative risk (RR) is approximately 40 times greater

- Early orchidopexy may protect against the development of malignancy
- The most common tumor that develops from a cryptorchid testis is ***seminoma***
- The cause of the increased risk for malignant degeneration of an undescended testis is at this time theoretical

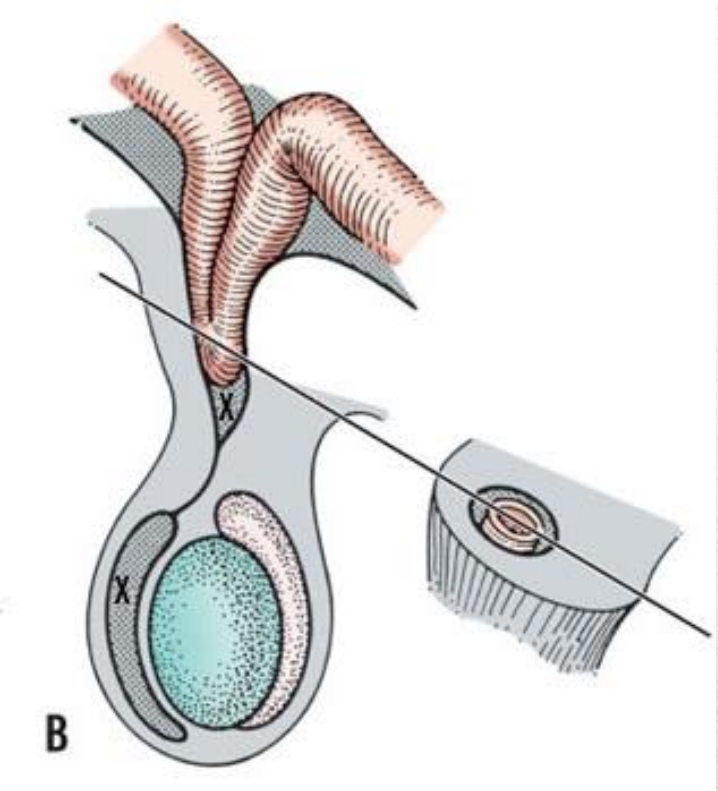
Congenital Hernia

- ***A patent processus vaginalis is found in more than 90% of patients with an undescended testis***

- The processus normally closes between the period after complete testicular descent and the first month after birth



Completely Patent



Partially Patent

Testicular Torsion

- The increased susceptibility of the testis to undergo torsion is the result of a developmental anatomic abnormality between the testis and its mesentery

- The mechanism is believed to be related to a greater relative broadness of the testicle than its mesentery...
  Scorer and Farrington, 1971

Diagnosis

- If the testes remains out of the scrotum at age 6 months confident diagnosis of congenital undescended testis can be made

Diagnosis of impalpable testes

- USG
- CT
- MRI
- Laparoscopy
- hCG stimulation

Treatments

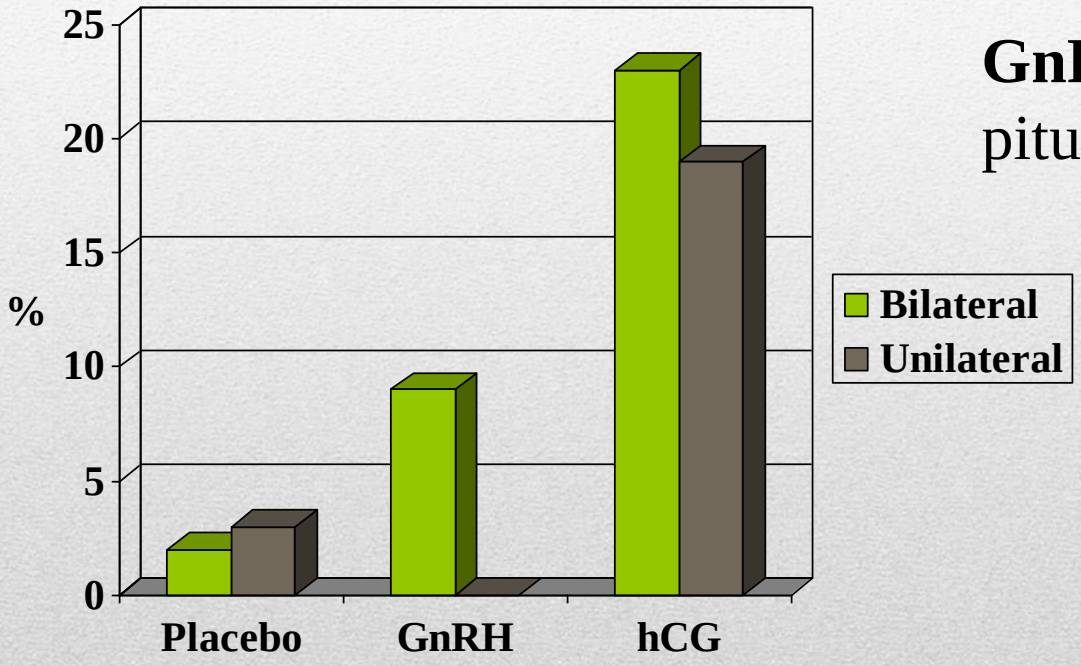
- **Definitive treatment of an undescended testis should take place between 6 and 12 months of age**

- Hormonal
  - hCG
  - GnRH
  - Combined (hCG & GnRH)
- Surgical

Rates of descent of the undescented testes following treatment. Christiansen 1992.

hCG (Stimulates Leydig cells)

GnRH (stimulates the pituitary to release LH)



Bilateral: p=0.0016
Unilateral: p=0.013

Hormonal Therapy

- the overall efficacy of hormonal treatment is less than 20% for cryptorchid testes and is significantly dependent on pretreatment testicular location

- Therefore***, surgery remains the gold standard*** for the management of undescended testes

Time of surgery

Ideal : 06 – 09 months or <1 year of age

Usually: between 1 and 3 years

- Degeneration of germ cells - at 6–12 months
- Morphological changes at EM - at 1–2 yr
- Light microscopic changes - at 3–4 yr
- Clinical atrophy of the testis - at 5–7 yr

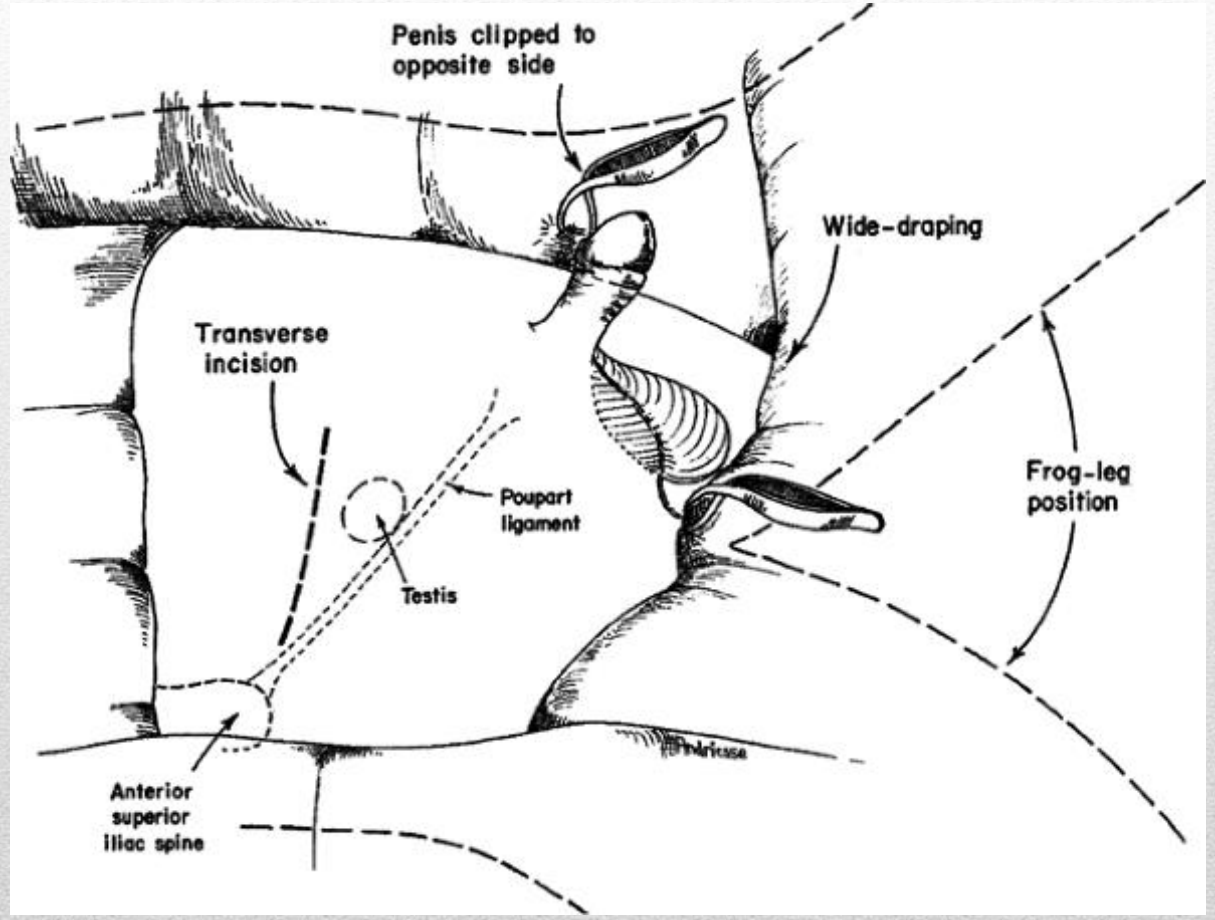
Surgical procedures

- **Orchidopexy**
- **A high inguinal or Jones and Bagley approach**
- **Laparoscopy - Fowler-Stephens Orchiopexy**
- **Orchidectomy**

Standard Orchiopexy

- complete mobilization of the testis and spermatic cord
- repair of the patent processus vaginalis by high ligation of the hernia sac
- skeletonization of the spermatic cord without sacrificing vascular integrity to achieve tension-free placement of the testis within the dependent position of the scrotum
- creation of a superficial pouch within the hemiscrotum to receive the testis

- A transverse inguinal skin incision is made in the midinguinal canal, usually in a skin crease

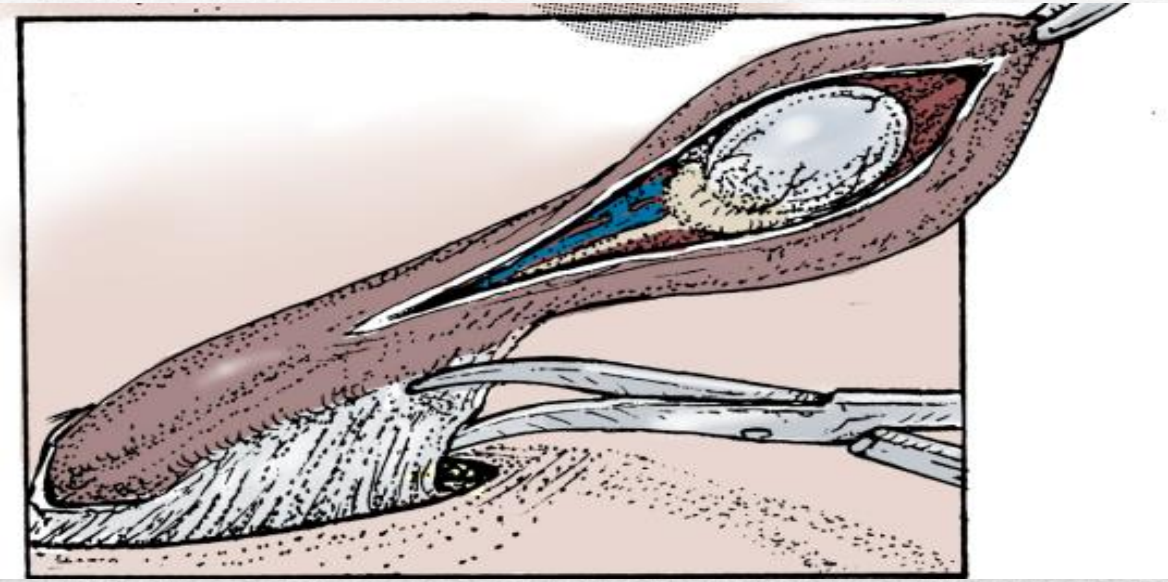


- Dissected in layers to expose the external oblique fascia

- the external oblique fascia is opened with a small superficial incision that is carried through the external ring

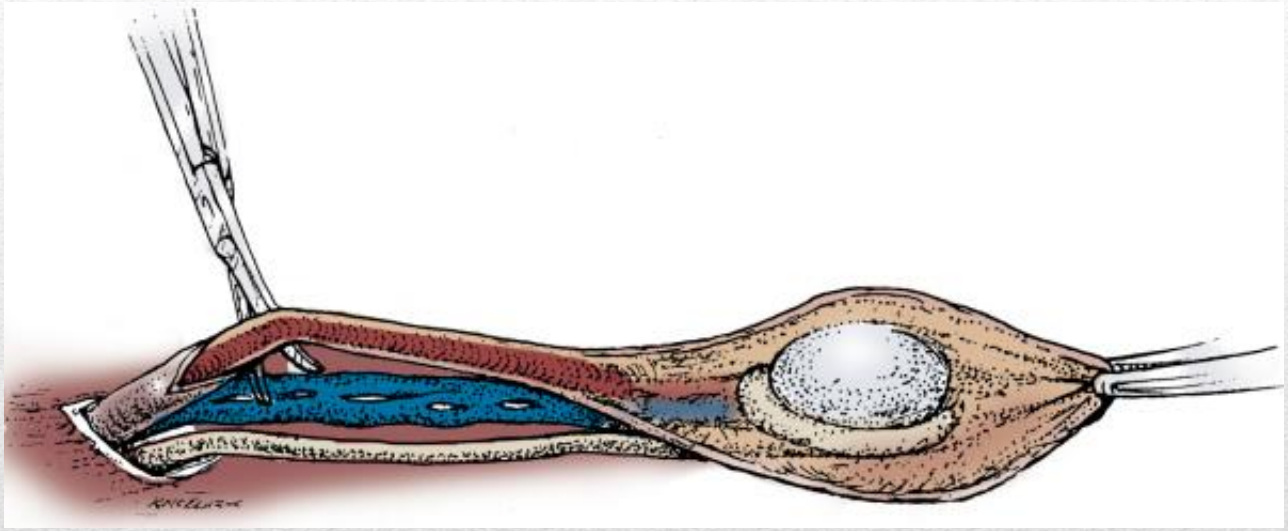
- The tunics overlying the testis are grasped and the distal gubernacular attachments are sharply dissected to free the testis up into the wound

- The cremasteric muscular fibers and any anomalous fibrous attachments are then dissected sharply away from the testis and spermatic cord



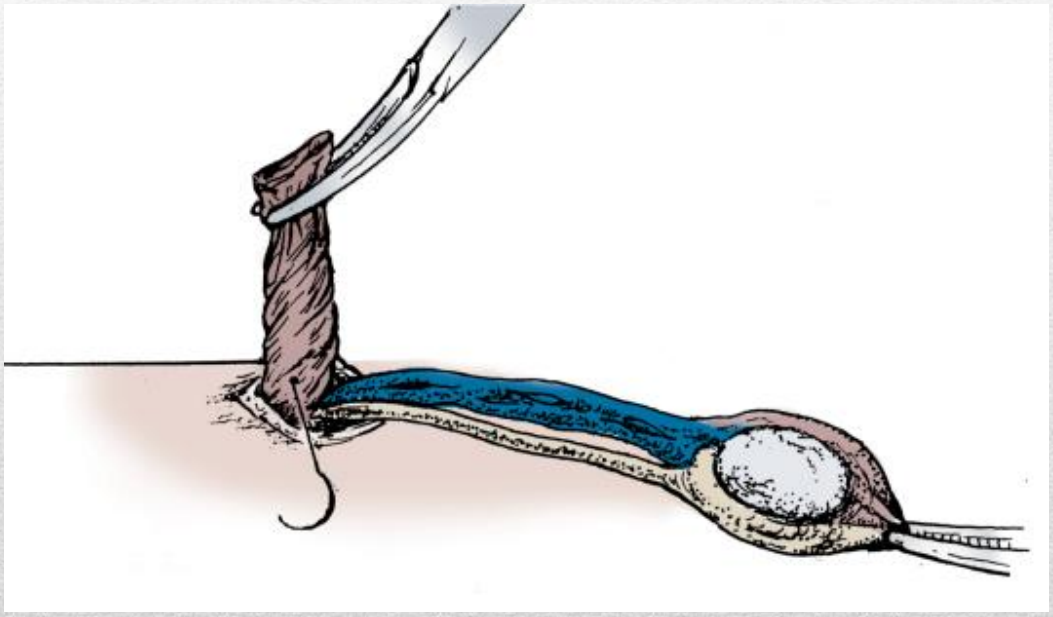
- Once the spermatic cord is freely mobilized to the internal ring, it is opened over the testis

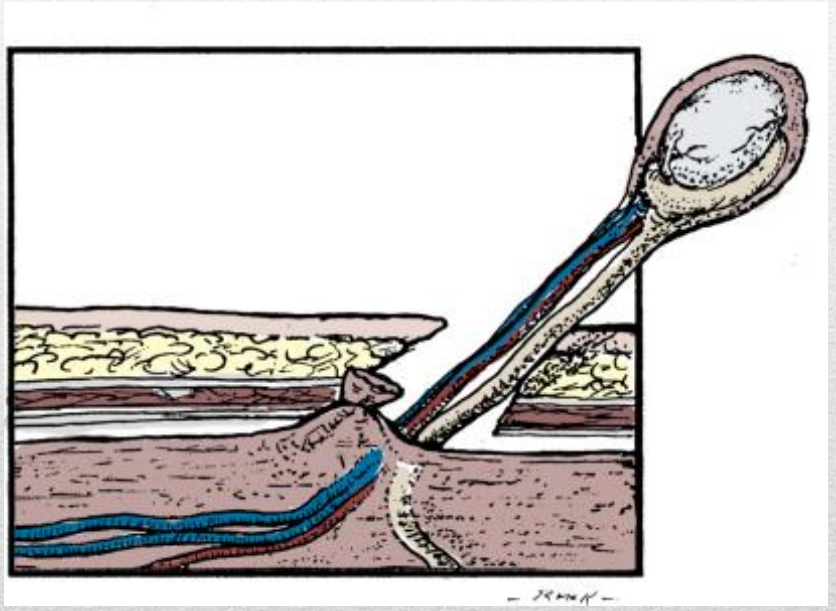
- the processus vaginalis is dissected and separated from the cord structures



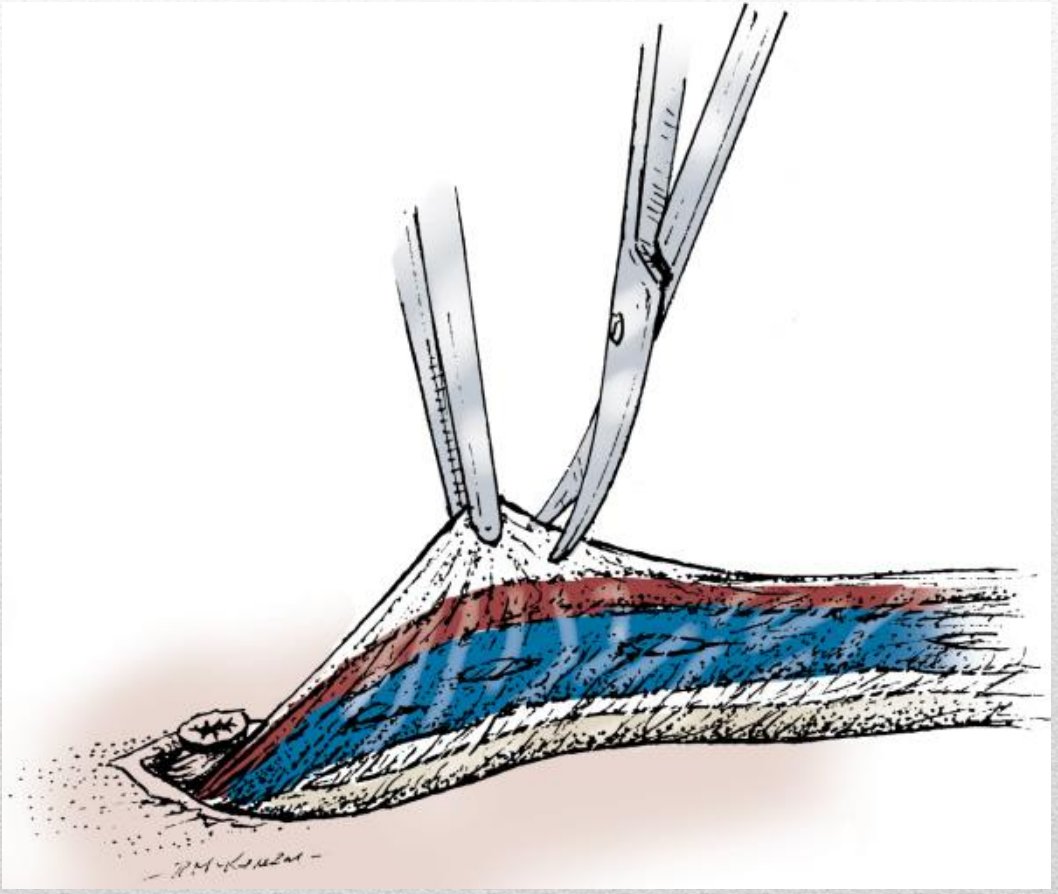
- In most cases, division of the processus vaginalis and cremasteric muscle attachments provides adequate cord length to allow for placement of the testis in the scrotum

- High ligation of the processus vaginalis at the internal inguinal ring is performed

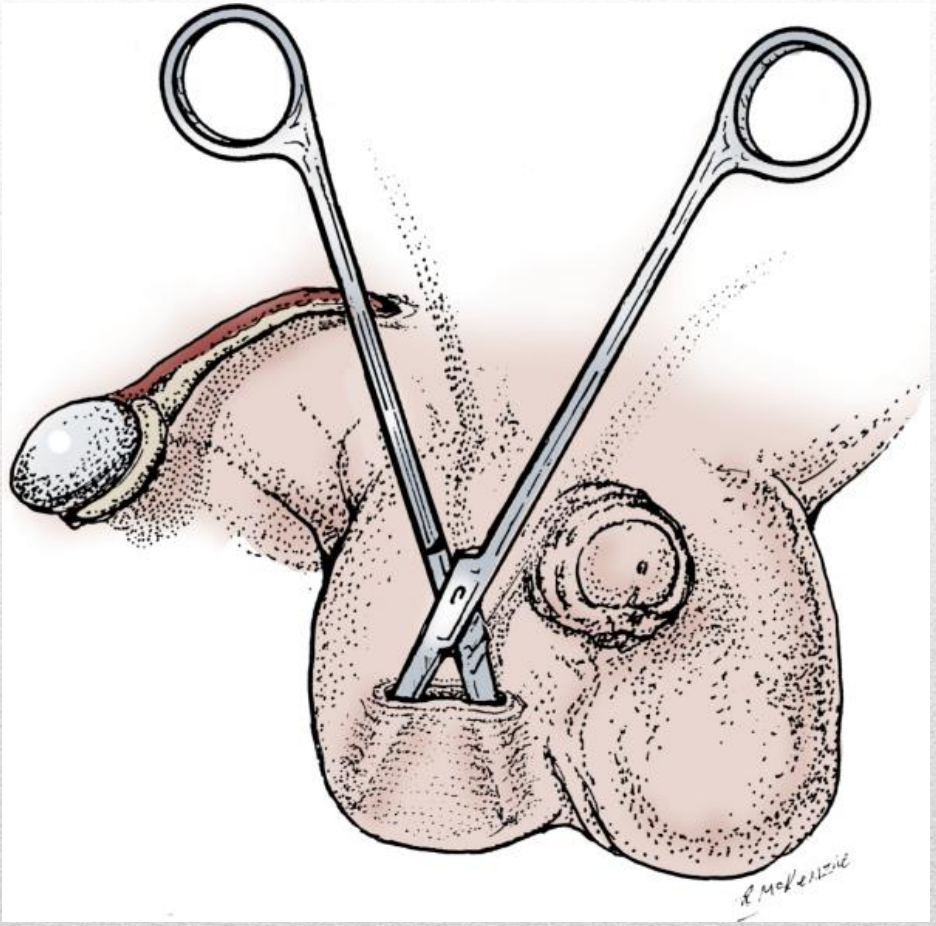




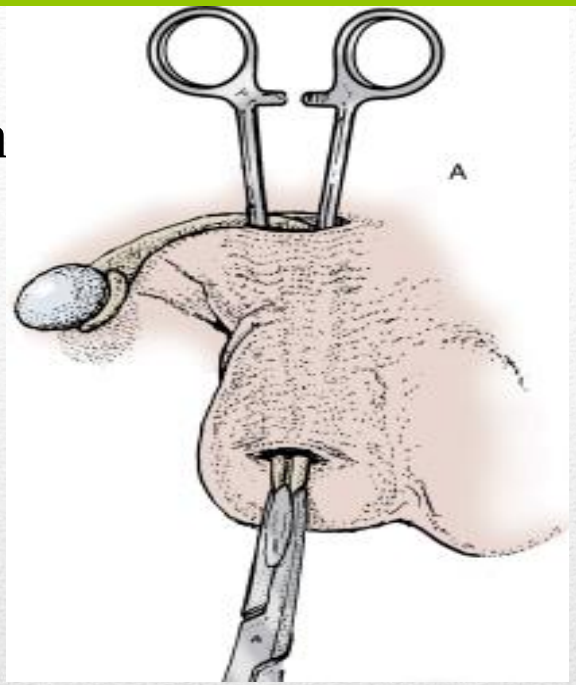
- after ligation of the processus vaginalis, the internal spermatic fascia is separated from the cord structures

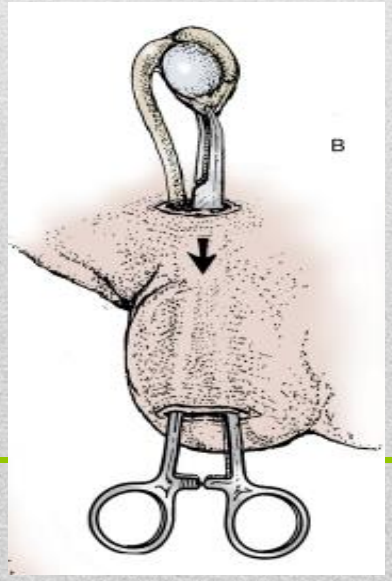


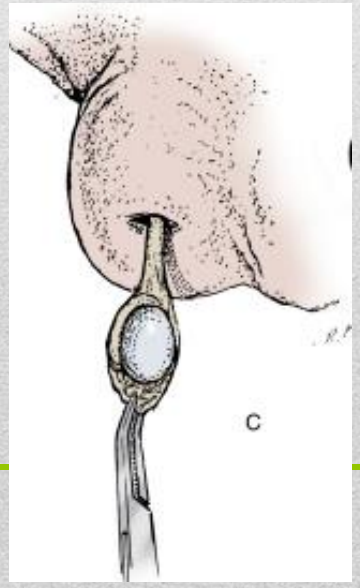
- The testis can be adequately and permanently secured in the scrotum by placement of the testis within a superficial dartos pouch
- results in complete circumferential adherence of the tunica albuginea to the scrotal skin
- A transverse midscrotal superficial skin incision is made within a rugal skin fold, and a mosquito hemostat is then used to develop a tissue plane just under the scrotal skin of the ipsilateral hemiscrotum



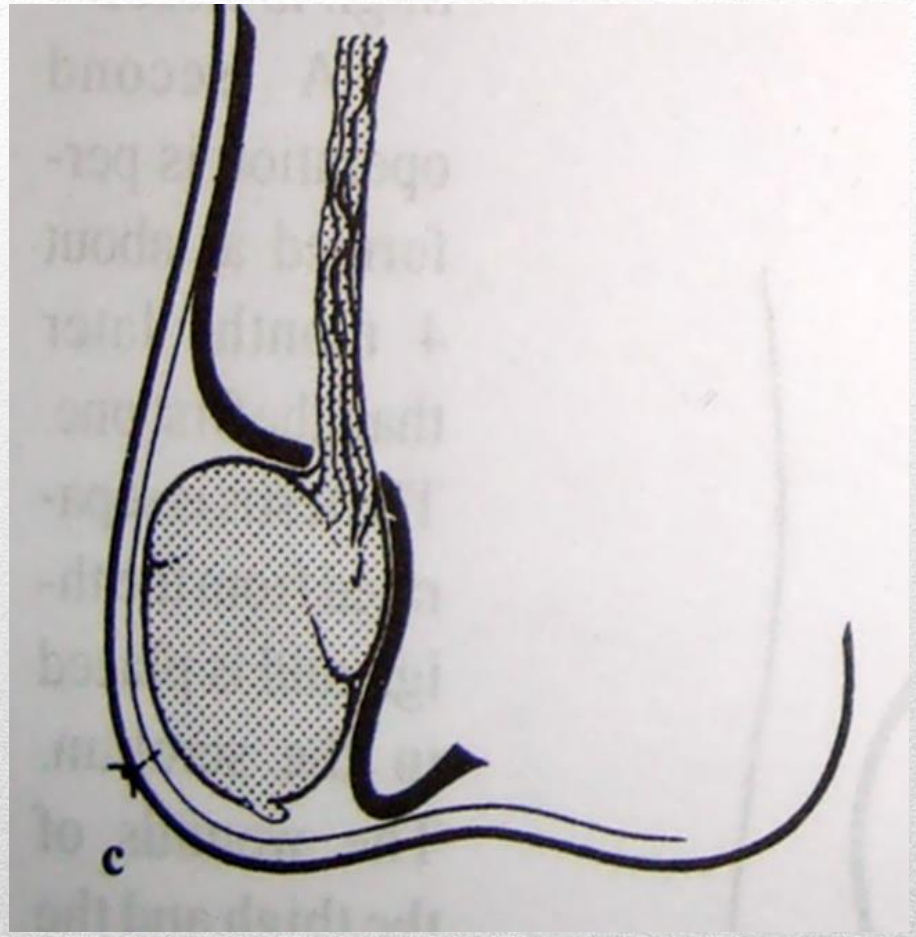
- Formation of a passage to the scrotum
- a pouch constructed between the dartos muscle and the skin
- the most dependent tunica vaginalis or remnant of gubernaculum is grasped, and the testis is passed into the scrotum



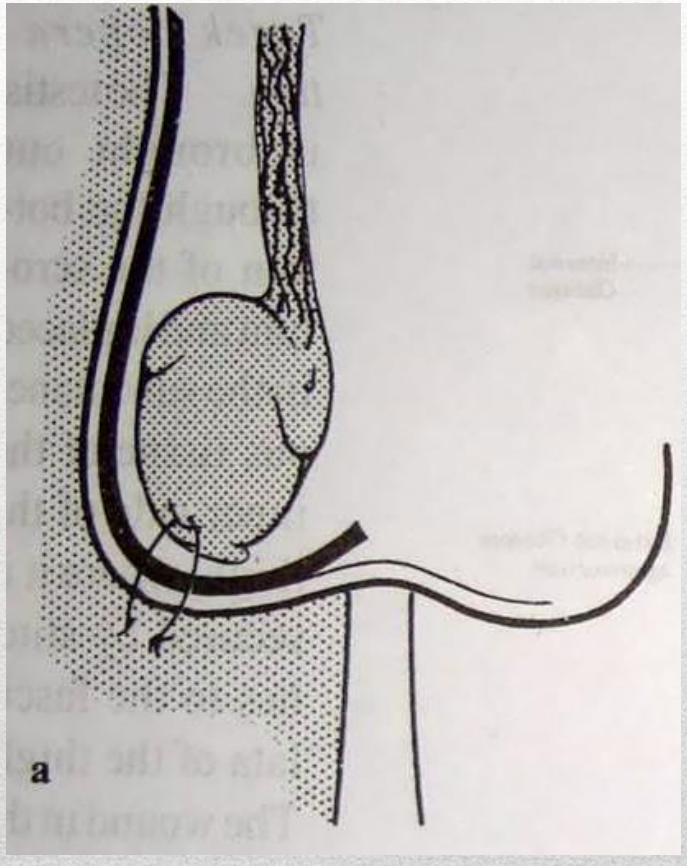




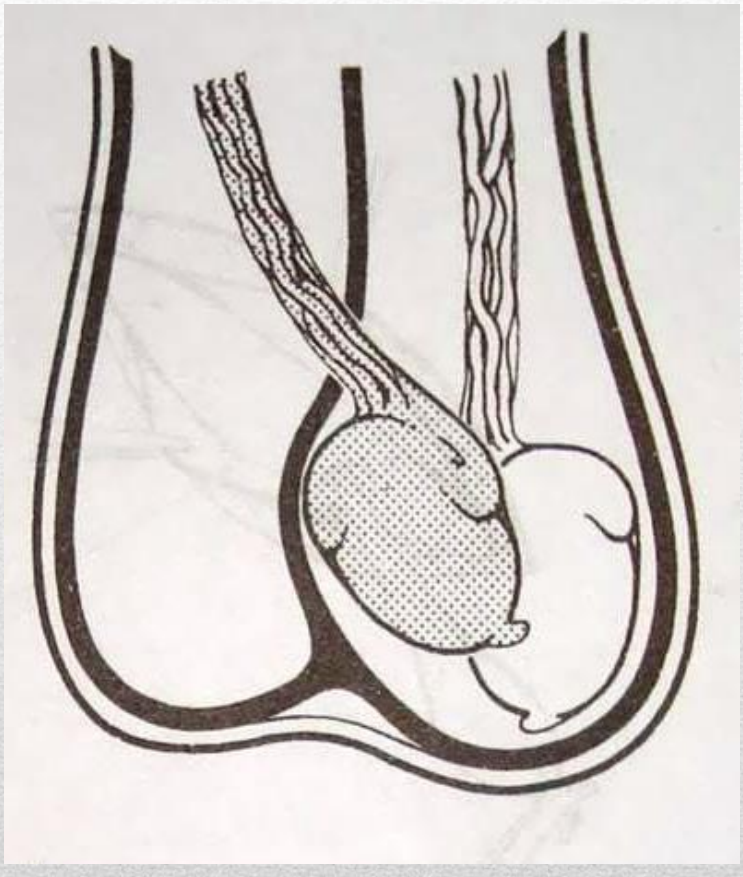
- The dartos fascial window is closed with fine absorbable suture, with the option of placing this suture through the redundant tunica vaginalis well above the level of the testis to indirectly secure the cord at this position
- The testis is then placed within the dartos pouch and the scrotal skin closed
- Inguinal incision is closed in layers



Other Fixation Techniques



External Anchorage



Ombrédanne's Operation

LAPAROSCOPY

- **Fowler-Stephens (one stage)**

  one stage procedure - mobilisation and fixation of the testes

- **Fowler-Stephens (two stage)**

  two stages procedure - ligation of the testicular vessels, mobilisation and fixation 6 months later

ECTOPIC TESTIS

- An ectopic testis completes normal transinguinal migration but is misdirected outside the normal path of descent below the external ring

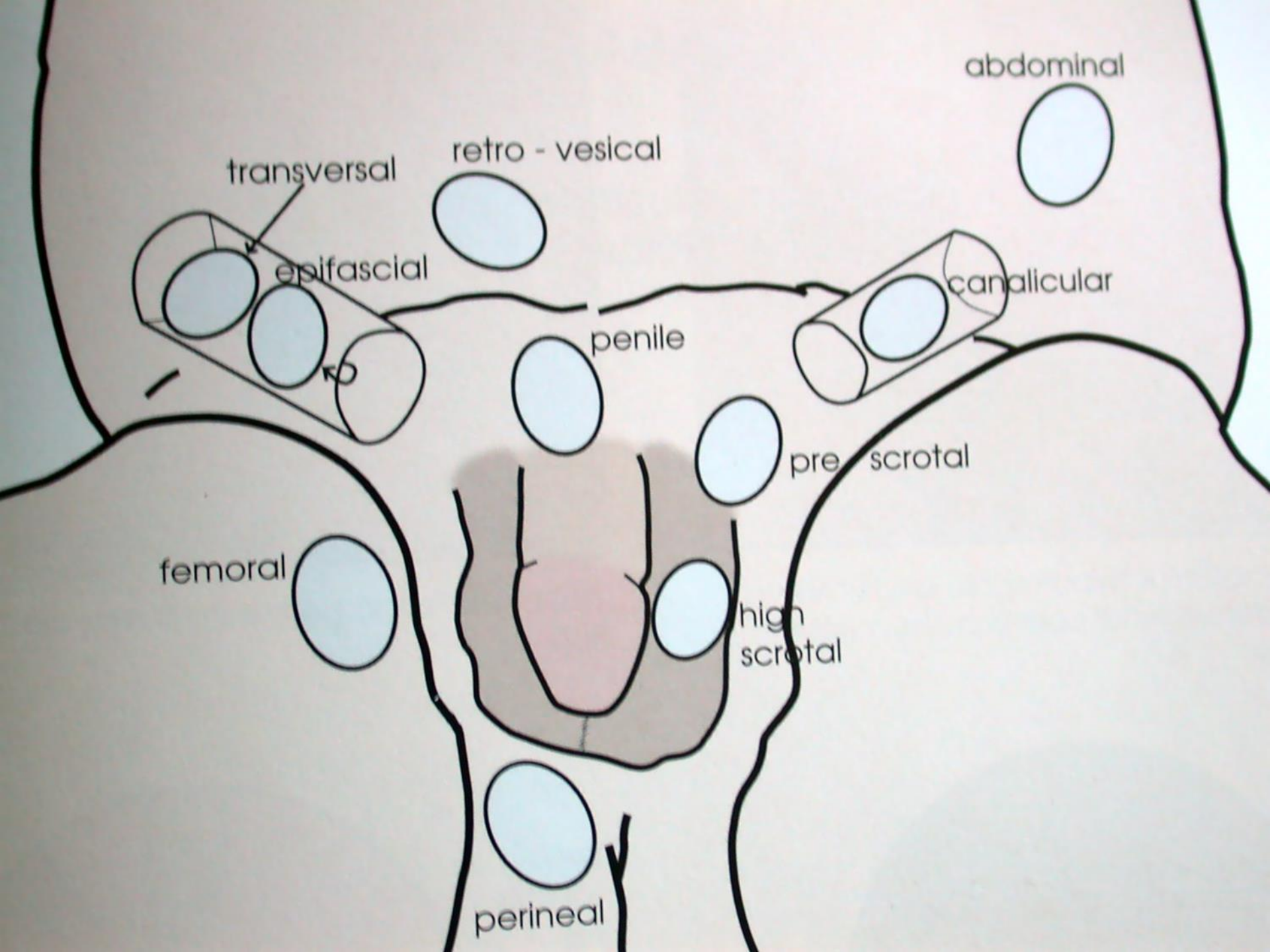
- The most common ectopic location is within a superficial pouch between the external oblique fascia and Scarpa's fascia, a structure that has been termed the Denis-Browne pouch

LOCKWOOD THEORY REGARDING ECTOPIC TESTIS

According to lockwood gubernacular band has four accessory tails called tails of lockwood

1.Superficial inguinal tail
2.Pubic tail
3.Perineal tail
4.Femoral tail

- Usually all tails disappear except scrotal tail.
- In ectopic testis scrotal tail weakens and ruptures and testis is pulled by any of accessory tails
- The term cryptorchidism covers both undescended and ectopic (maldescended) testes. Both should be located and placed in the scrotum at an early age if at all possible


abdominal
retro - vesical
transversal
epifascial
canalicular
penile
pre - scrotal
femoral
high scrotal
perineal

- Other abnormal locations include transverse scrotal, femoral, perineal, and prepenile ectopia
- An ectopic testis is usually fully developed
- The main hazard is liability to injury

Comparison between ectopic & undescended testis

Undescended testis

- The testis is arrested in its normal path of descent
- Usually undeveloped
- Undeveloped & empty scrotum on the affected side
- Shorter length of spermatic cord
- Poor spermatogenesis after 6 yrs
- Usually associated with indirect inguinal hernia
- Treatment: surgery & HT
- Associated with a number of complications

Ectopic testis

- The testis deviates from its normal path of descent
- Fully developed testis
- Empty but usually fully developed scrotum
- Longer length of spermatic cord
- Spermatogenesis is perfect
- Never associated with indirect inguinal hernia
- Treatment: basically surgical
- Complications: liability to injury

Retractile Testis

- A "retractile testis" withdraws spontaneously out of the scrotum toward the inguinal canal by an active cremasteric reflex but can easily be brought down into a dependent position within the scrotum and remains there after traction has been released

- The risk of ascent may be as great as 50% in children with a "significantly" retractile testis

- If a testis can be milked down to the bottom of the scrotum, it is probably retractile and does not require therapy.... Wyllie, 1984

- They are normal and **require no treatment**
- Will descend at puberty
- Rarely - ***Cremasterotomy***

ASCENDED TESTIS

- The “ascending testis” is defined as a testis that resides in the scrotum in early infancy but is too high later in childhood
- Delayed descent in the first 12 weeks after birth, with subsequent ascent out of the scrotum, is a common feature
- Boys previously documented to have normally descended testes are found later in childhood to be cryptorchid
- Therefore, children with retractile testes should be monitored regularly (yearly), at least up to puberty, until the testes are no longer retractile and remain intrascrotal

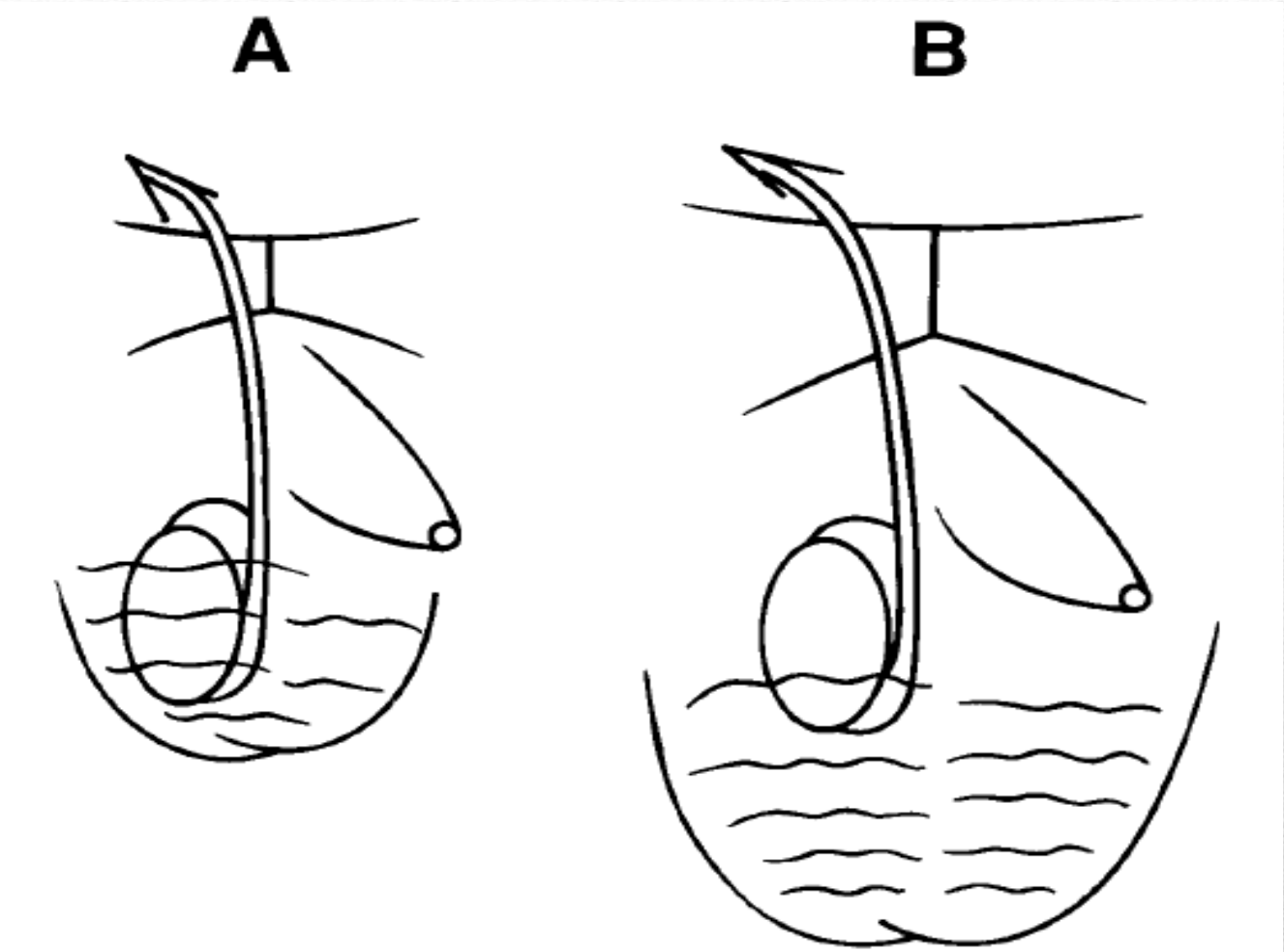


FIG. 19. Failure of the spermatic cord to elongate in proportion to body growth may be a cause of "ascending" or "retractile" testes. The testis that is fully descended in infancy (A) assumes a relatively higher position later in childhood (B). [Reproduced with permission from J. M. Hutson and S. W. Beasley: *Descent of the Testis*, 1992 (149)].

- A **vanishing or absent testis** is usually encountered during exploration for a Nonpalpable testis
- The anatomic hallmark of a vanishing testis is blind-ending spermatic vessels that are found just proximal to the internal inguinal ring
- The most likely cause for this is prenatal torsion
- True agenesis of the testis is rarer.
- Laparoscopy is useful in distinguishing these causes of clinically absent testis from intra-abdominal maldescent

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INTERNET

Thank You