

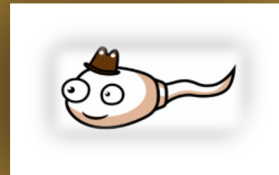


Surgical Treatment of **Infertile Male**

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 **Wake Forest[®]**
School of Medicine

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Disclosures

Drs. Sadri, Howards and Dutta have *no financial disclosures or conflicts of interest* to report relevant to this presentation.

Learning objectives

After this presentation, the learner should be able to :

- Perform the appropriate evaluation and surgical treatment of the male in an infertile couple.**
- Apply the latest recommendations of AUA/ASRM on surgical management of the male in an infertile couple.**

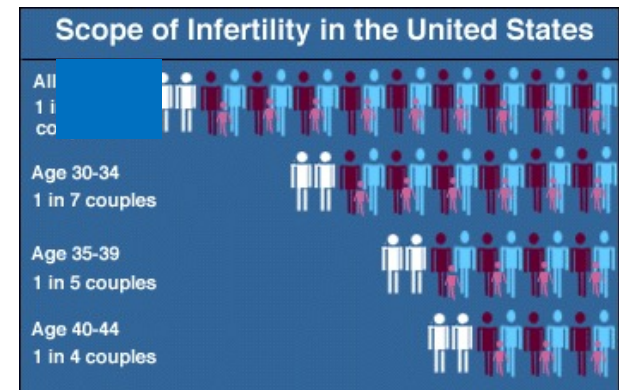
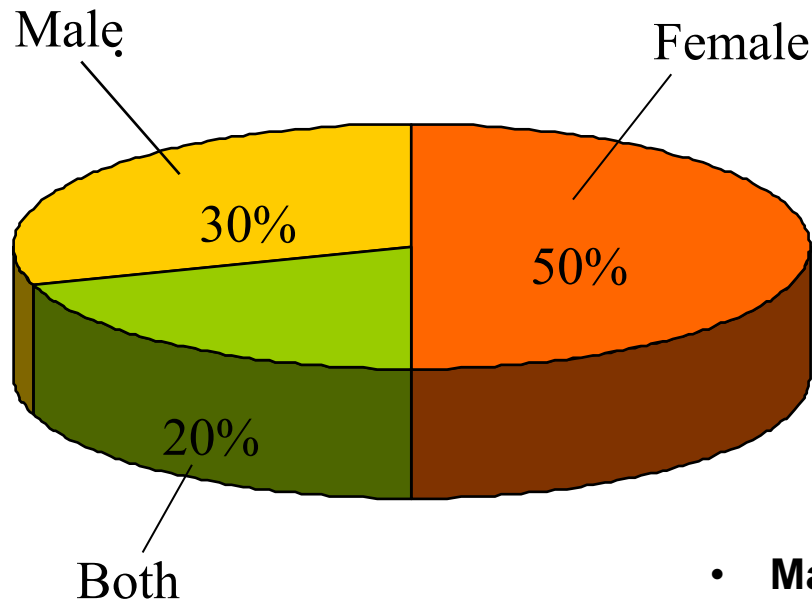
AUA Nomenclature Linking Statement Type to Level of Certainty, Magnitude of Benefit or Risk/Burden, and Body of Evidence Strength

	Evidence Strength A (High Certainty)	Evidence Strength B (Moderate Certainty)	Evidence Strength C (Low Certainty)
Strong Recommendation (Net benefit or harm substantial)	Benefits > Risks/Burdens (or vice versa) Net benefit (or net harm) is substantial Applies to most patients in most circumstances and future research is unlikely to change confidence	Benefits > Risks/Burdens (or vice versa) Net benefit (or net harm) is substantial Applies to most patients in most circumstances but better evidence could change confidence	Benefits > Risks/Burdens (or vice versa) Net benefit (or net harm) appears substantial Applies to most patients in most circumstances but better evidence is likely to change confidence (rarely used to support a Strong Recommendation)
Moderate Recommendation (Net benefit or harm moderate)	Benefits > Risks/Burdens (or vice versa) Net benefit (or net harm) is moderate Applies to most patients in most circumstances and future research is unlikely to change confidence	Benefits > Risks/Burdens (or vice versa) Net benefit (or net harm) is moderate Applies to most patients in most circumstances but better evidence could change confidence	Benefits > Risks/Burdens (or vice versa) Net benefit (or net harm) appears moderate Applies to most patients in most circumstances but better evidence is likely to change confidence
Conditional Recommendation (No apparent net benefit or harm)	Benefits = Risks/Burdens Best action depends on individual patient circumstances Future research unlikely to change confidence	Benefits = Risks/Burdens Best action appears to depend on individual patient circumstances Better evidence could change confidence	Balance between Benefits & Risks/Burdens unclear Alternative strategies may be equally reasonable Better evidence likely to change confidence
Clinical Principle	A statement about a component of clinical care that is widely agreed upon by urologists or other clinicians for which there may or may not be evidence in the medical literature		
Expert Opinion	A statement, achieved by consensus of the Panel, that is based on members' clinical training, experience, knowledge, and judgment for which there is no evidence		



Male and Female Infertility

- No conception after 1 yr of unprotected sexual intercourse is defined as possible infertility
- 85% of couples conceive within 1 yr
- 50% of infertility involves male factor.



http://library.med.utah.edu/kw/human_reprod/seminars/seminar2A.html

- **Male infertility is a problem in 7% of all men**

Goals of Medical and Surgical Treatments

- The goal of the therapeutic attempts to optimizing the male potential fertility can be one of following:
 1. To help the couple to achieve a **spontaneous pregnancy**.
 2. To use a **less invasive** method of assisted reproduction like conventional intrauterine insemination (IUI) or in-vitro fertilization (IVF) instead of intracytoplasmic sperm injection (ICSI).
 3. To improve the **success rate** from either method of assisted reproduction.

Assisted Reproductive Technology

IUI

5 million motile sperm

Intra-uterine
Insemination



IVF

75,000 motile sperm

In Vitro
Fertilization



ICSI

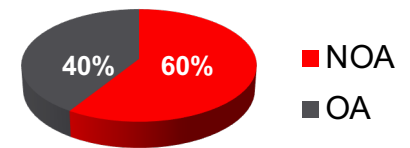
~20 motile sperm

Intracytoplasmic Sperm
Injection



Azoospermia

- **Definition:** Complete **absence** of spermatozoa in the **ejaculate**, in at least **two** semen samples after extended preparation including **centrifugation**.
- **Prevalence:**
 - **1% of male population**
 - **10-15 % of men undergoing evaluation for infertility**
- **Etiology Classifications:**
 - **I (more accurate)**
 - Genital tract obstruction ■ Deficient spermatogenesis ■ Hypogonadotropic hypogonadism
 - **II (Less accurate)**
 - Obstructive Azoospermia (OA) ■ Non-Obstructive Azoospermia (NOA)



OBSTRUCTIVE AZOOSPERMIA

EJACULATORY DUCT OBSTRUCTION

5% of Azoospermia

ETIOLOGIES OF OBSTRUCTION

- **CONGENITAL** and utricular or
- **ACQUIRED** (etiologies)

Congenital

- Agenesia
- Stenosis
- Prostatic utricular cyst
- Müllerian cyst
- Wolffian cyst

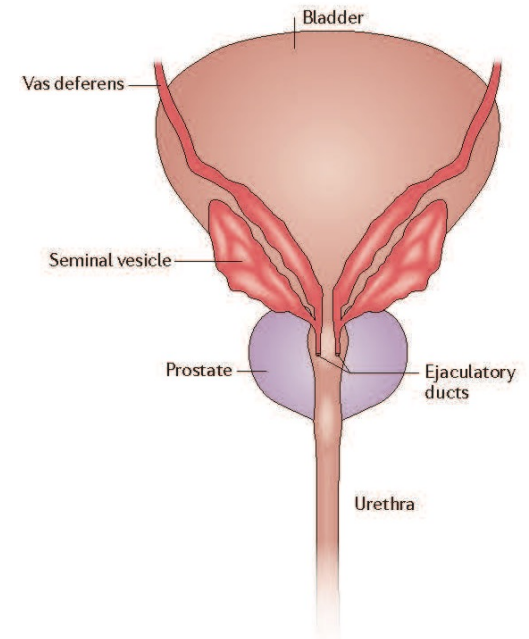
Acquired

- Trauma or iatrogenic lesion
 - Endoscopic resection
 - Excision of seminal cysts
 - Rectal surgery in childhood
- Infection
 - Genital infection
 - Urinary infection
 - Prostatic abscess
 - Prolonged catheterization
 - Tuberculosis
- Post-infectious calculus
- Neoplasia

Idiopathic

ejaculatory d

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OBSTRUCTIVE AZOOSPERMIA

- **EJACULATORY DUCT OBSTRUCTION**

5% of Azoospermia

- **Anatomy**

- **ETIOLOGY**

-
-

- **SYMPTOMS**

- **SIGNS**

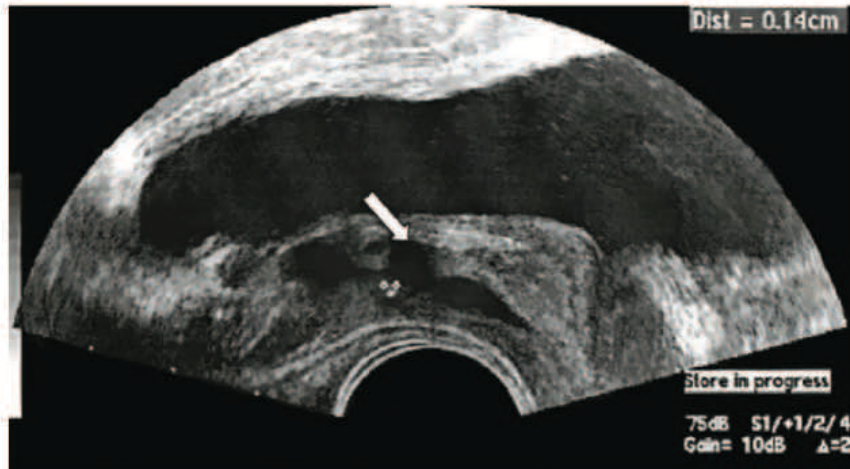
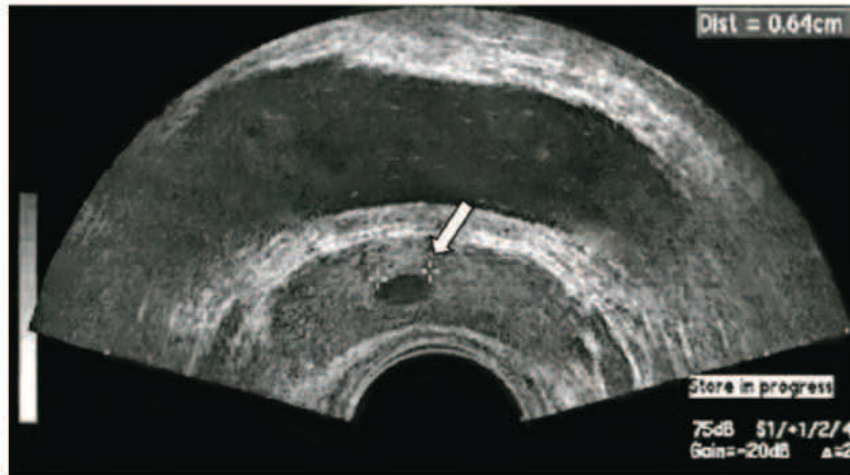


Figure 1 Transrectal Ultrasound (TRUS): coronal and sagittal sections. Note the dilated seminal vesicles (white arrow).

OBSTRUCTIVE AZOOSPERMIA

EJACULATORY DUCT OBSTRUCTION

5% of Azoospermia

- Anatomy
- ETIOLOGIE
 - CONGI and utric
 - ACQUI etiologie
- SYMPTOM
- SIGNS (EX

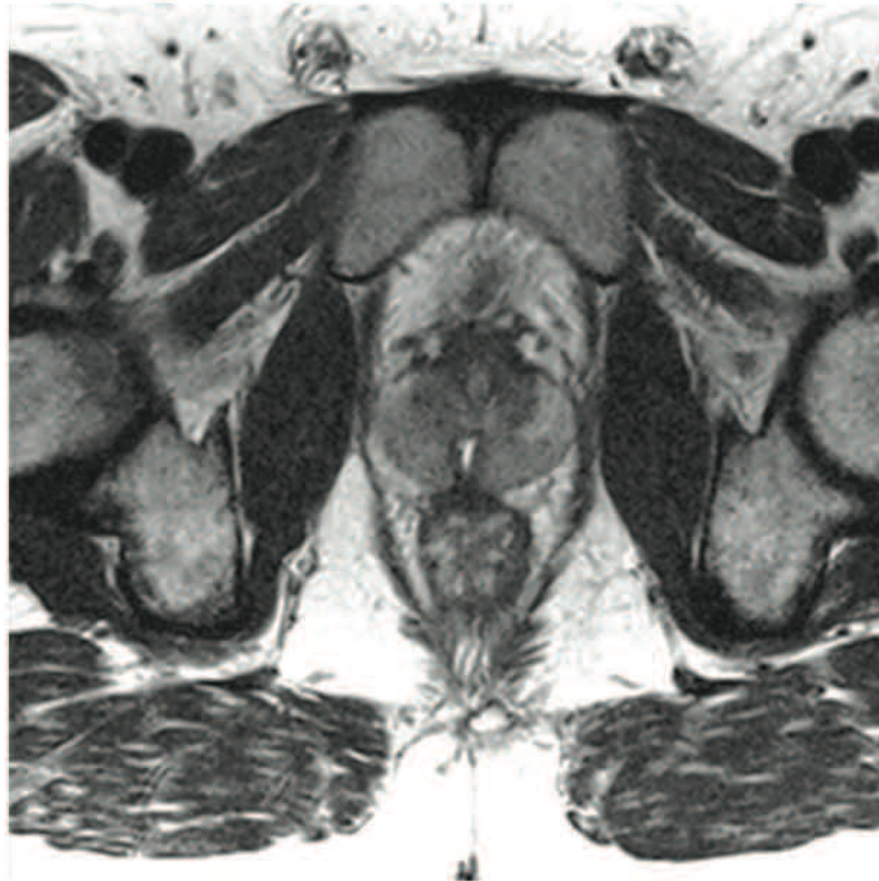
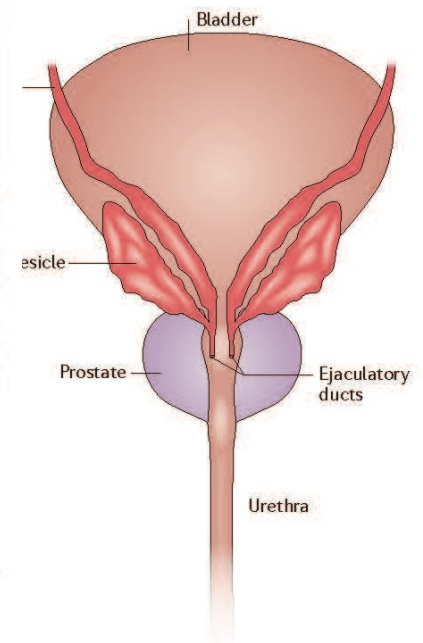


Figure 3 | MRI scan of a midline cyst. T2-weighted axial cross-section image of a midline ejaculatory duct cyst.

y ducts,
trogenic



OBSTRUCTIVE AZOOSPERMIA

- **EJACULATORY DUCT OBSTRUCTION**

5% of Azoospermia

- **ETIOLOGIES OF OBSTRUCTION**

- **CONGENITAL** (atresia or stenosis of the ejaculatory ducts,

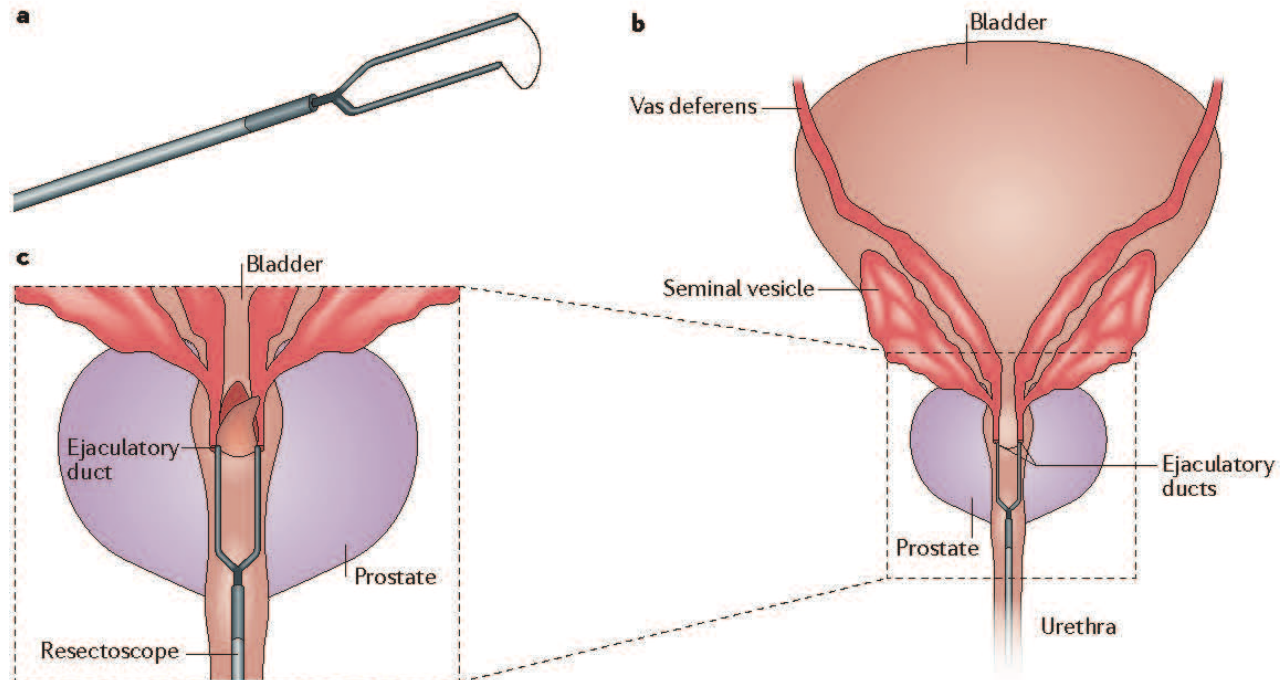


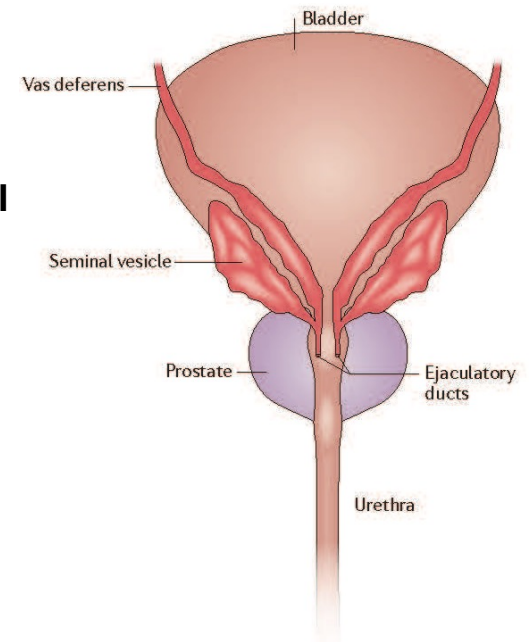
Figure 5 | The surgical approach in transurethral ejaculatory duct resection (TURED). a | The TURED procedure uses a resectoscope wire loop, inserted via the urethra. b | The resectoscope approaches the opening of the ejaculatory ducts within the prostatic urethra. c | Loop resection deroofs the midline ejaculatory duct cyst.

OBSTRUCTIVE AZOOSPERMIA

- **EJACULATORY DUCT OBSTRUCTION**

5% of Azoospermia

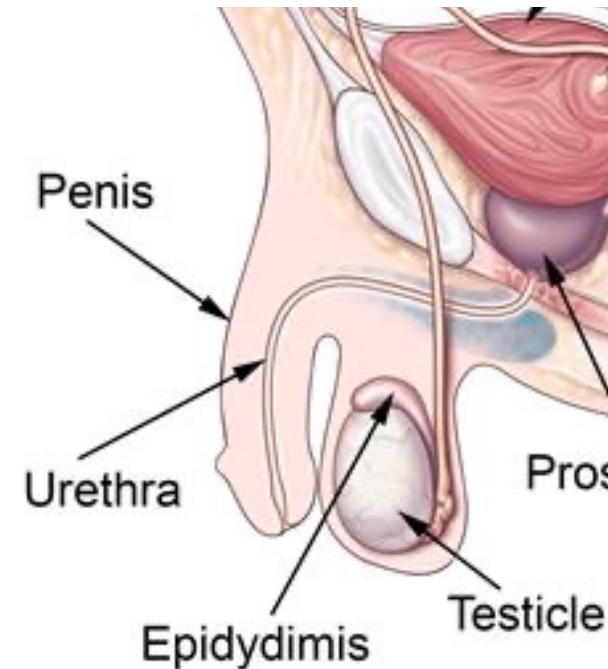
- **Anatomy**
- **ETIOLOGIES OF OBSTRUCTION**
 - **CONGENITAL** (atresia or stenosis of the ejaculatory ducts, and utricular or Wolffian)
 - **ACQUIRED** (trauma, inflammation, infection, and iatrogenic etiologies)
- **SYMPTOMS** (most of the nothing!)
- **SIGNS (EXAMINATION, IMAGING):** TRUS, MRI
- **TREATMENT** (TURED, PESA, TESA, TESE)



OBSTRUCTIVE AZOOSPERMIA

EPIDIDYMAL AND VASAL OBSTRUCTION

- **ETIOLOGIES OF OBSTRUCTION**
 - **CONGENITAL**
 - **ACQUIRED**



OBSTRUCTIVE AZOOSPERMIA

EPIDIDYMAL AND VASAL OBSTRUCTION

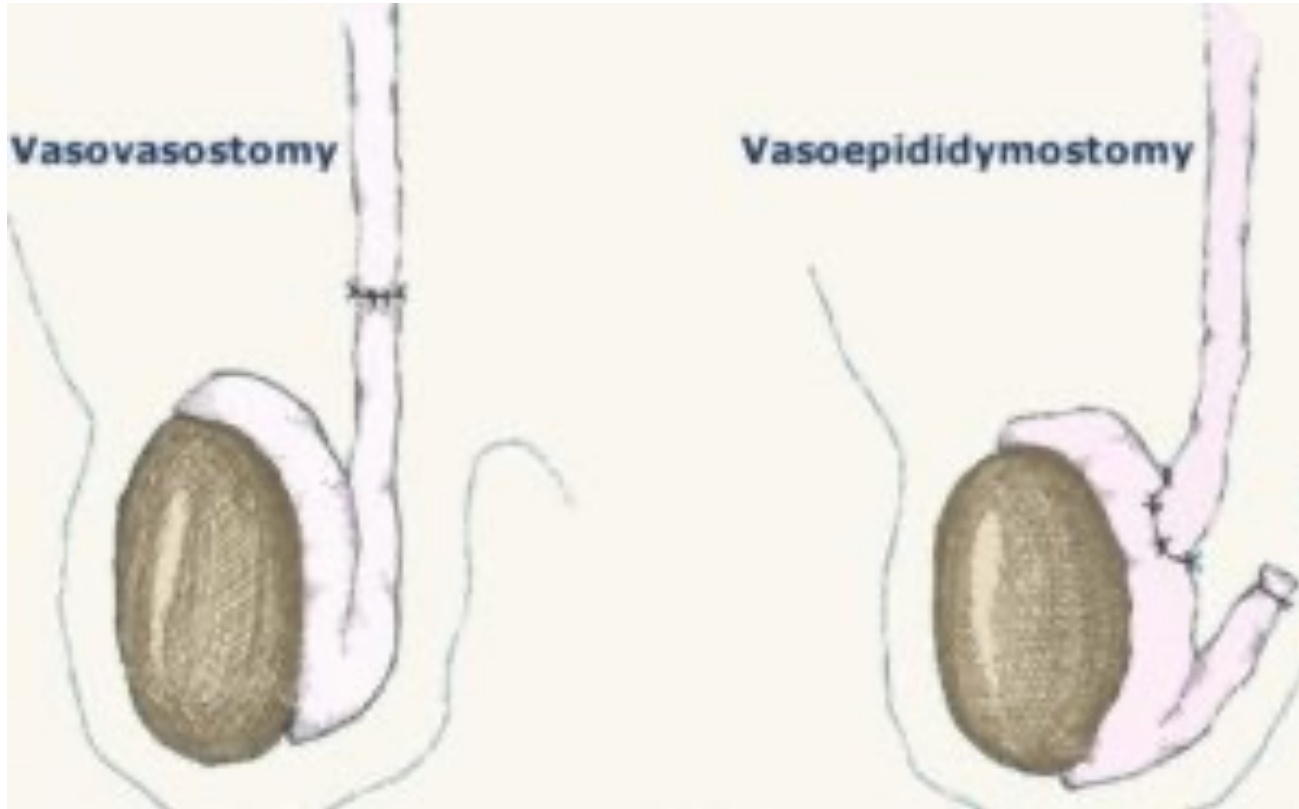
- **ETIOLOGIES OF OBSTRUCTION**
 - **CONGENITAL** (CBAVD "Cystic Fibrosis", idiopathic epididymal obstruction)
 - **ACQUIRED**
 - Traumatic injury of the epididymis (typically iatrogenic e.g., post hydrocelectomy or orchidopexy).
 - Infectious or inflammatory damage. The obstruction may also be secondary to chronic vasal obstruction (post vasectomy), associated with back pressure induced rupture of the epididymal tubule.
 - Many cases are idiopathic.
 - Surgery for epididymal cyst is also a reported cause of obstruction.
 - Silent chronic infection by Chlamydia trachomatis, although a common etiology of epididymitis, is an uncommon cause of male reproductive tract obstruction, unlike what is seen for women.

OBSTRUCTIVE AZOOSPERMIA

EPIDIDYMAL AND VASAL OBSTRUCTION

- **ETIOLOGIES OF OBSTRUCTION**
 - **CONGENITAL**
 - **ACQUIRED**
- **SIGNS (EXAMINATION, IMAGING)**
- **TREATMENT (Vasovasostomy, Vasoepididymostomy, TESA, TESE)**

Vasectomy Reversal



Vasovasostomy

- The results of vasovasostomy are better after **microsurgical** than after **macrosurgical** anastomosis
- Microsurgical vasovasostomy was described by Dr. Owen and popularized by Dr. Silber in 1976



- Multiple modifications were introduced, all based on the surgical principles of a tension free, watertight anastomosis with mucosa-to-mucosa apposition.
- Prior to performing microsurgery in the male, the female partner should be evaluated to determine if female infertility actors are present.
- Hormonal evaluation of men prior to vas reversal (T, E2, FSH, LH)

Vasovasostomy

- After a scrotal incision, the two ends of the vas are excised and the patency of the distal end is tested with injection of saline solution
- The fluid obtained from the proximal or testicular end is observed, and from its gross and microscopic appearance as well as the surgeon's experience, a decision to perform vasovasostomy or vasoepididymostomy is made.

Table 2. Vasal Fluid Grading, and Surgical Recommendation Based on Gross Appearance of Vasal Fluid and Microscopic Findings

Grade	Microscopic findings	Vasal fluid appearance	Surgical procedure recommended
1	Mainly normal motile sperm	Copious, cloudy, water soluble	Vasovasostomy
2	Mainly normal non motile sperm	Copious, cloudy, water soluble	Vasovasostomy
3	Mainly sperm head	Copious, cloudy, water soluble	Vasovasostomy
4	Only sperm head	Copious, cloudy, water insoluble	Vasovasostomy
5	No sperm	Copious, crystal clear, watery	Vasovasostomy
5	No sperm	Copious, thick white toothpaste-like, water insoluble	Vasoepididymostomy
5	No sperm	Scant white thin fluid	Vasoepididymostomy

If the vas fluid has a thick, creamy consistency it should be diluted with normal saline to allow observation of sperm that otherwise may be overlooked because they are packed together tightly, and obscured by debris in the viscous fluid.

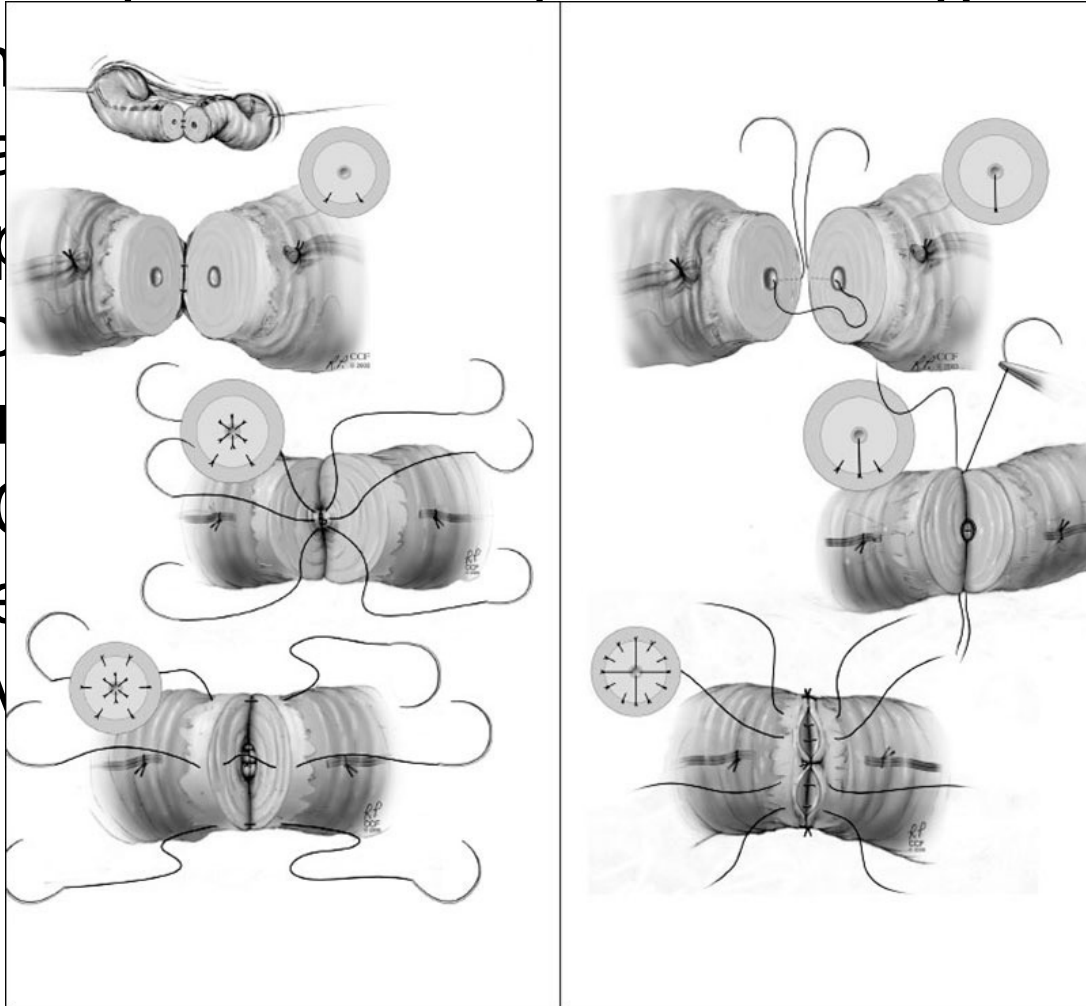
Vasovasostomy

- A one-layer or two-layer microsurgical

technique
similar

- Cryopreservation
intraoperative
patient
IVF/ICSI

- There are
vasovasostomy
are performed

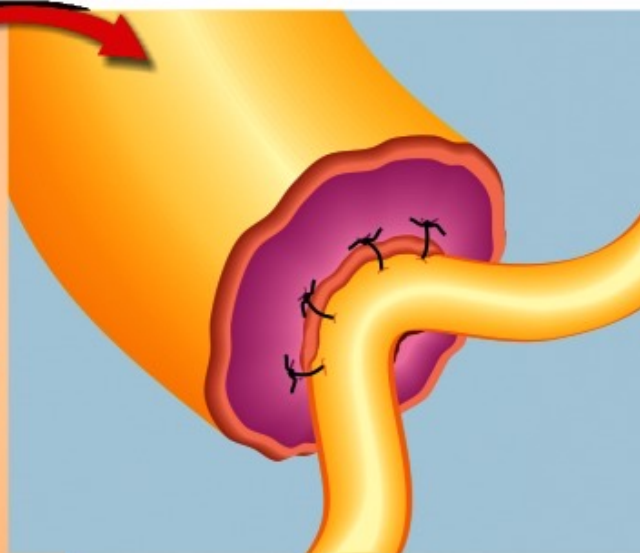
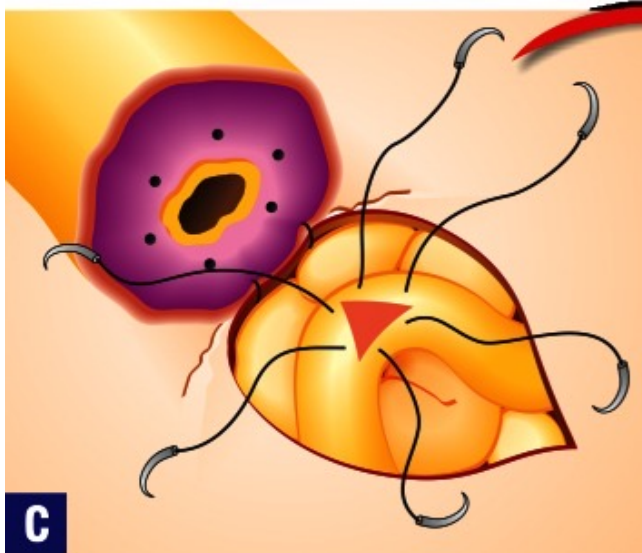
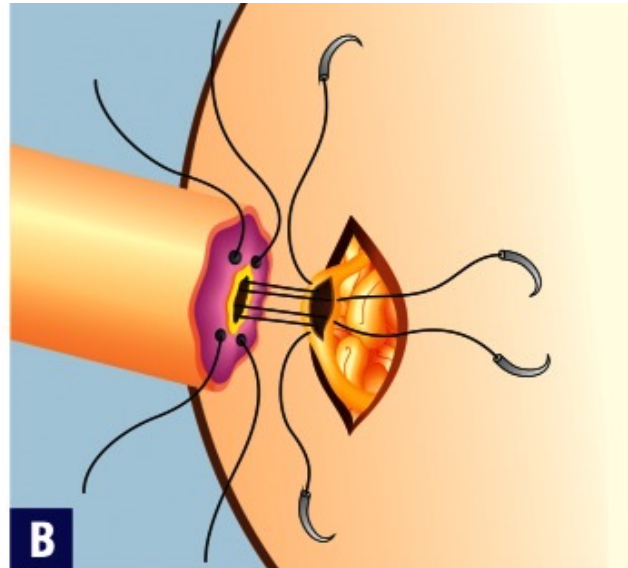
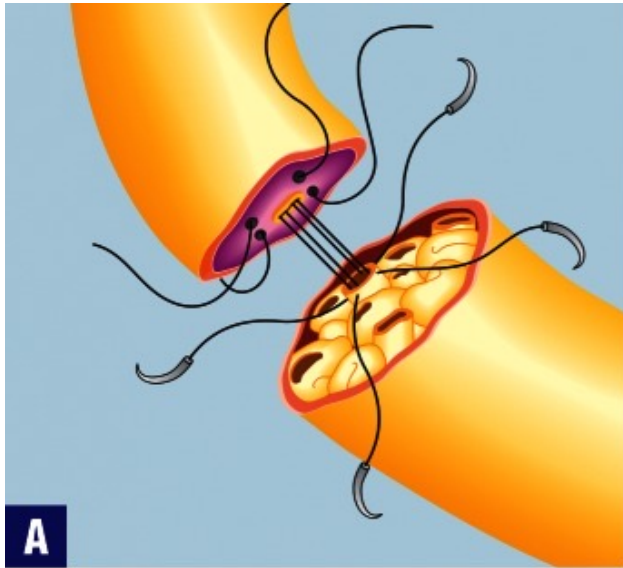


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Vasoepididymostomy



Vas Reversal Patency and Pregnancy

Table 18.1: Vasovasostomy outcomes³⁰

<i>Obstructive interval (years)</i>	<i>Patency rates (%)</i>	<i>Pregnancy rates (%)</i>
< 3	97	76
3-8	88	53
9-14	79	44
≥ 14	71	30

- Semen analyses are performed three months after the intervention and repeated at that frequency until sperm parameters are normal or pregnancy occurs.
- Cryopreservation should be considered when motile sperm return to the ejaculate.
- For bilateral vasovasostomy, the overall patency rate is 87% and the pregnancy rate is 53%, and for bilateral vasoepididymostomy, overall patency rate is 50% and pregnancy rate is 29%.

Sperm Granuloma and VR outcome

- A grossly identifiable sperm granuloma occurs in 15% to 40% of men after a vasectomy.
- This immune reaction to leaking sperm at the cut end of the vas was thought to have a positive effect on vasovasostomy outcome.
- The granuloma is thought to benefit the reconstruction by allowing sperm leakage to be reabsorbed within the microcanaliculi of the sperm granuloma, preventing secondary pressure buildup and damage to the epididymis.
- The Vasovasostomy Study Group showed that patency and pregnancy rates **are not significantly** different whether or should be taken into account when counseling couples regarding the more appropriate treatment



RECOMMENDATION

- Couples desiring conception **after vasectomy** should be counseled that surgical reconstruction, surgical sperm retrieval, or both reconstruction and simultaneous sperm retrieval for cryopreservation are viable options. (Moderate Recommendation; Evidence Level: Grade C)
- Clinicians should counsel men with vasal or epididymal obstructive azoospermia that **microsurgical reconstruction** may be successful in returning sperm to the ejaculate. (Expert Opinion)
- For infertile men with azoospermia and EDO, the clinician may consider transurethral resection of ejaculatory ducts (**TURED**) or surgical sperm extraction. (Expert Opinion)

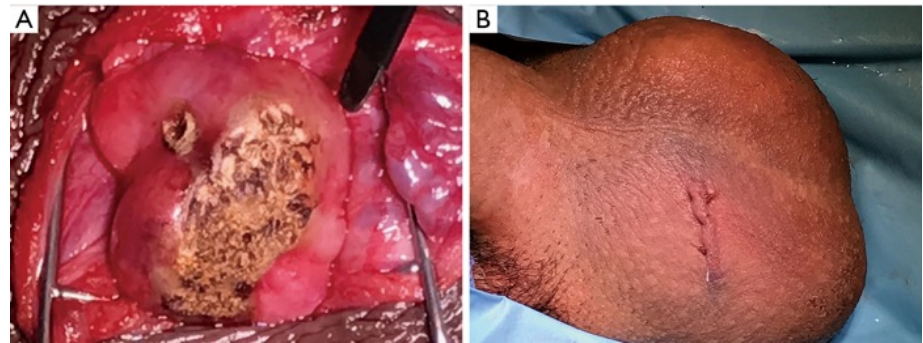
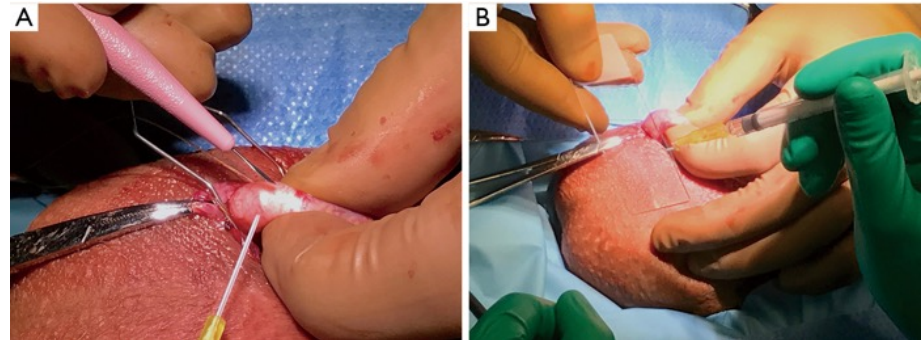
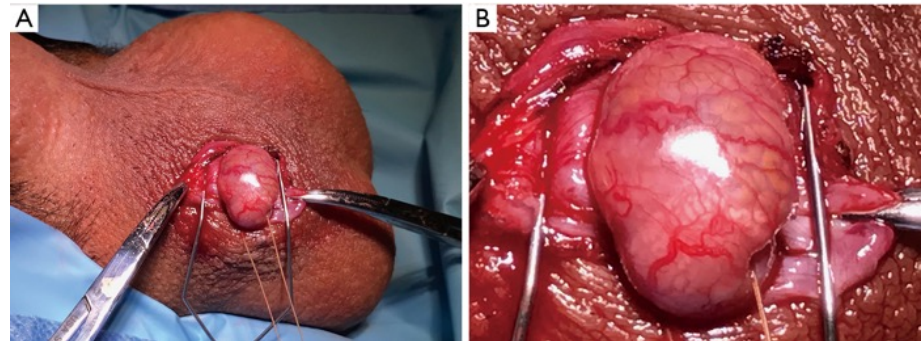
Surgical sperm retrievals



Surgical sperm retrievals

- **Microepididymal Sperm Aspiration (MESA)**

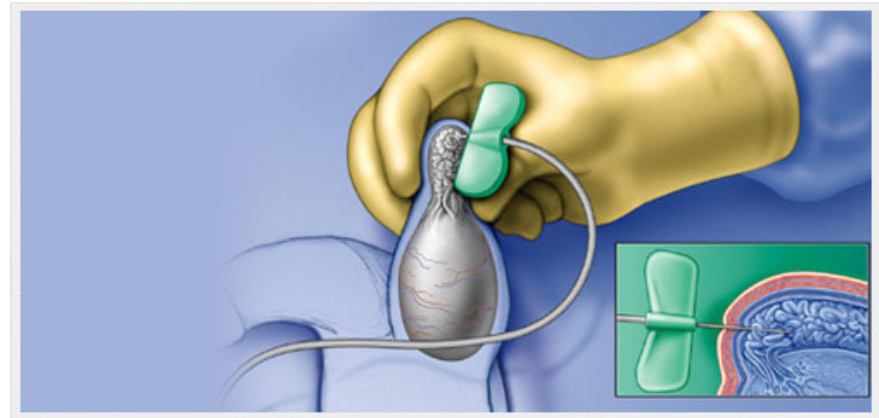
minimally invasive
epididymal sperm
aspiration (MIESA)



Complications of MESA are extremely rare and similar to those related to any scrotal exploration, such as pain, hematoma, and infection.

Surgical sperm retrievals

- **PERCUTANEOUS EPIDIDYMAL SPERM ASPIRATION (PESA)**



- Anesthetic infiltration of the spermatic chord
- The caput epididymis is held between the surgeon's fingers and a 21G Butterfly needle is inserted into the epididymis
- PESA is a relatively safe procedure, but it is not entirely free from complications such as epididymal fibrosis, localized pain, and intra scrotal hematomas
- Actually, in 10% of cases no spermatozoa can be retrieved and their number is often inadequate for cryopreservation.
- In addition, pregnancy rates per cycle (19–34%) are found to be overall lower than with MESA (>40%).

Surgical sperm retrievals

- **Testicular Fine Needle Aspiration (TeFNA)**
- **Testicular Sperm Aspiration (TESA)**

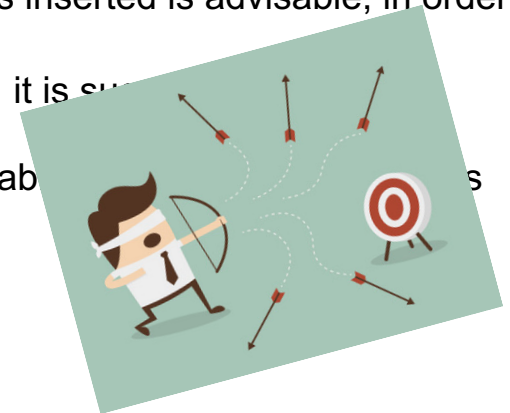
18-21-G Butterfly™ needle attached to a 20-mL plastic syringe



14-18 G Bard® Monopty® Instrument



- Anesthesia, the needle is directly inserted into the testicular tissue various times
- After needle removal, maintaining a moderate pressure where the needle was inserted is advisable, in order to facilitate hemostasis.
- In cases of NOA, TeFNA results in very low retrieval rates, such as 10-21.1%. it is successful exclusively in cases of severe hypospermatogenesis
- In addition, TeFNA only allows a cytological examination, therefore it is not suitable for in situ and testicular malignancies



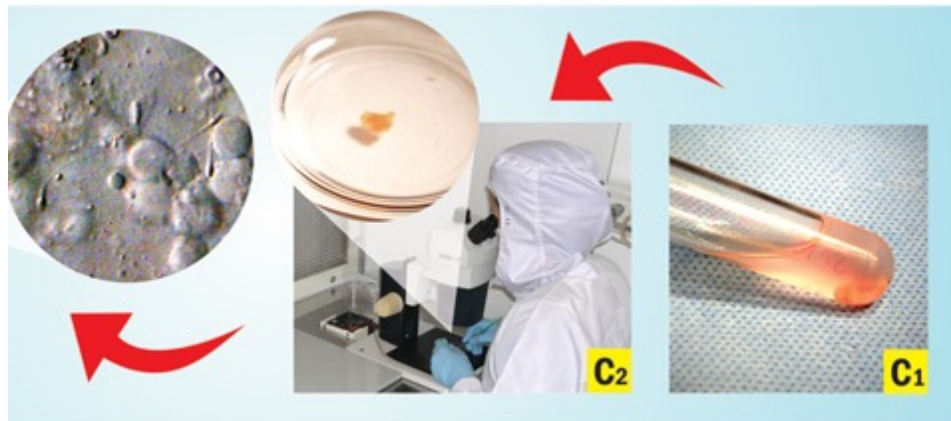
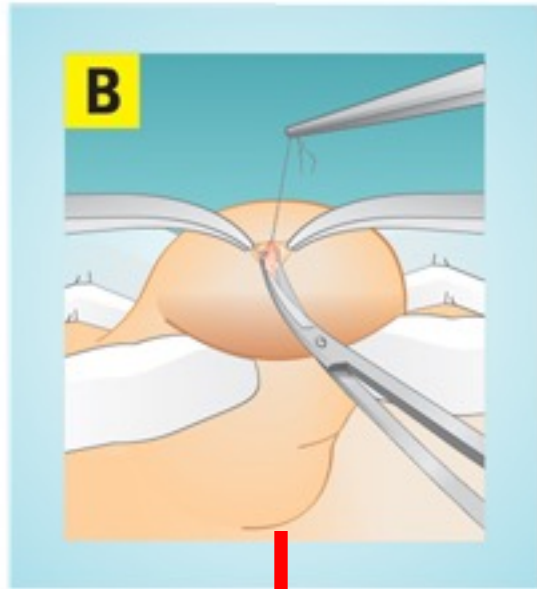


Surgical sperm retrievals

Conventional Testicular Sperm Extraction (c-TESE)

- **Alternative name (s):** Open Testicular Biopsy (TESE)
- **Advantage:** higher sperm recovery than TESA (FNA), less expensive than Micro-TESE
- **Disadvantage:** more expensive than TESA (FNA), more invasive than TESA (FNA)
- **Techniques:** loco-regional anesthesia with light sedation or general anesthesia, opening tunica vaginalis, transverse albugineotomy (5-10mm), controlling hemostasis, closing the albugineotomy, the tunica vaginalis, the dartos, and the skin (repeat in multiple sites).

Conventional Testicular Sperm Extraction (c-TESE)



- *Sperm Retrieval Rate (%)*: 40-50%.
- *Complications (rare)*:
 - **Infection** and **bleeding** with scrotal hematomas (rarely require surgical drainage).
 - In cases of NOA patients with very small testes, **testosterone deficiency** following surgery must be considered.

Clinical Andrology 2011, EAU/ESAU Course Guidelines; Edited by L Björndahl, A Giwercman, H Tournaye and W Weidner



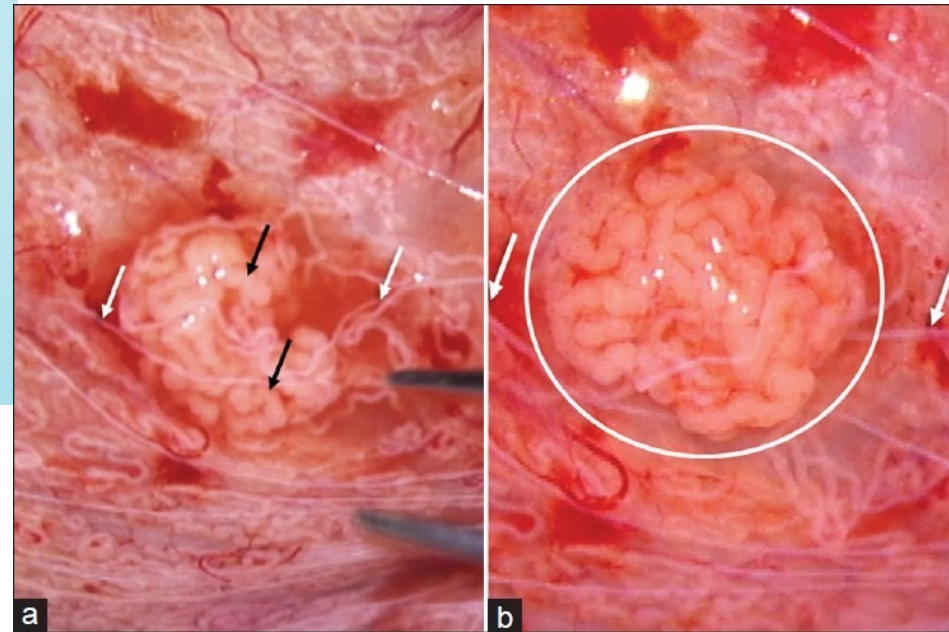
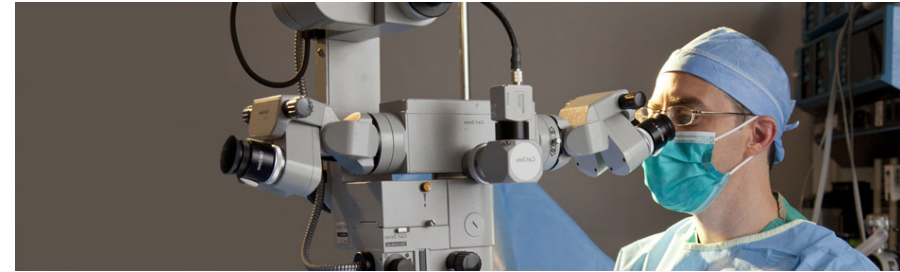
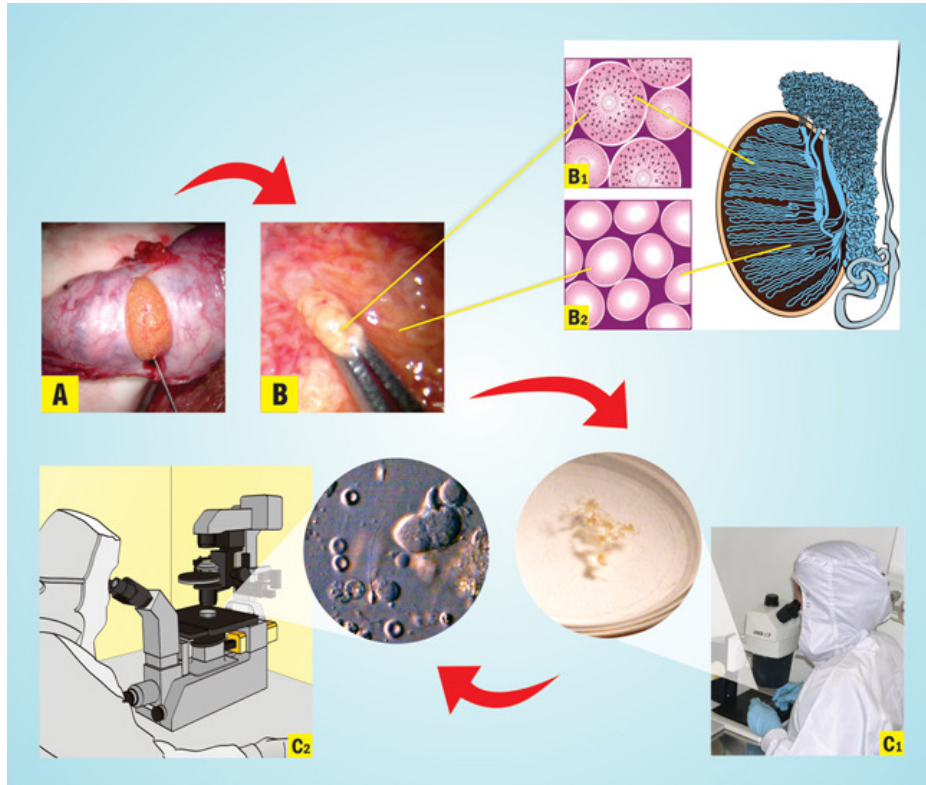
Peter Schlegel

Surgical sperm retrievals

Microscopic Testicular Sperm Extraction (Micro-TESE)

- *Alternative name (s):* **Microdissection (MD)**
- *Advantage:* less testicular trauma and scar tissue than cTESE (removal of smaller amount of testicular tissue).
- *Disadvantage:* more expensive than c-TESE), more invasive than TESA (FNA).
- *Techniques:* general or spinal anesthesia, opening of the testicle by means of an equatorial or longitudinal incision, removal of single tubules observed to have the largest diameter under an operating microscope (**20-25X** magnification) or, in the **absence** of larger tubules, of those **closest** to vessels and at different depths in the pulp.

Microscopic Testicular Sperm Extraction (Micro-TESE)



Clinical Andrology 2011, EAU/ESAU Course Guidelines; Edited by L Björndahl, A Giwercman, H Tournaye and W Weidner

Microscopic Testicular Sperm Extraction (Micro-TESE)

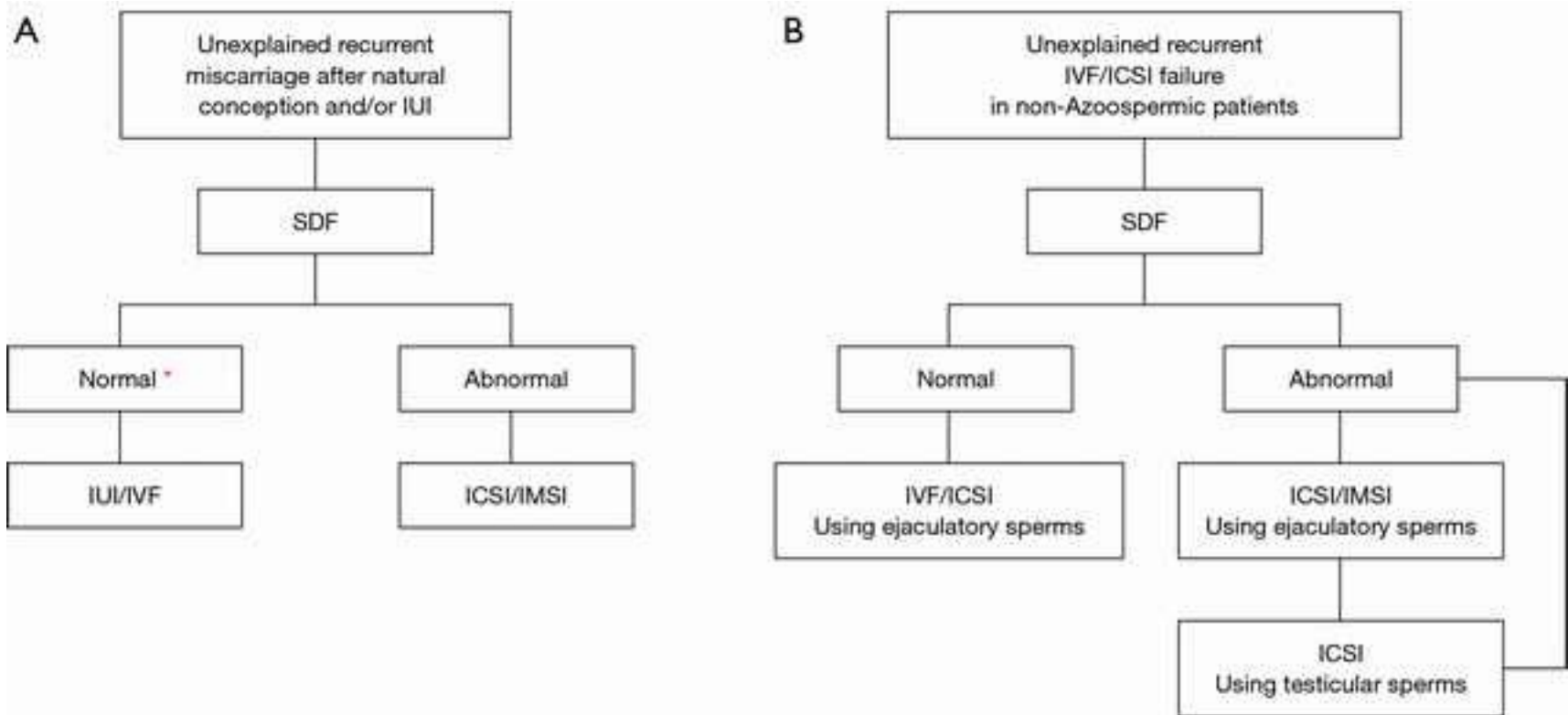
- *Sperm Retrieval Rate (%)*: 40-70%.
- *Complications (rare)*: The same as cTESE, **less** testicular tissue is removed, thus greatly reducing the risk of endocrine deprivation. Moreover, there appear to be significantly **fewer vascular** complications than with TESE; at **six-month** ultrasound follow up **no** parenchymal or vascularization abnormalities were reported.



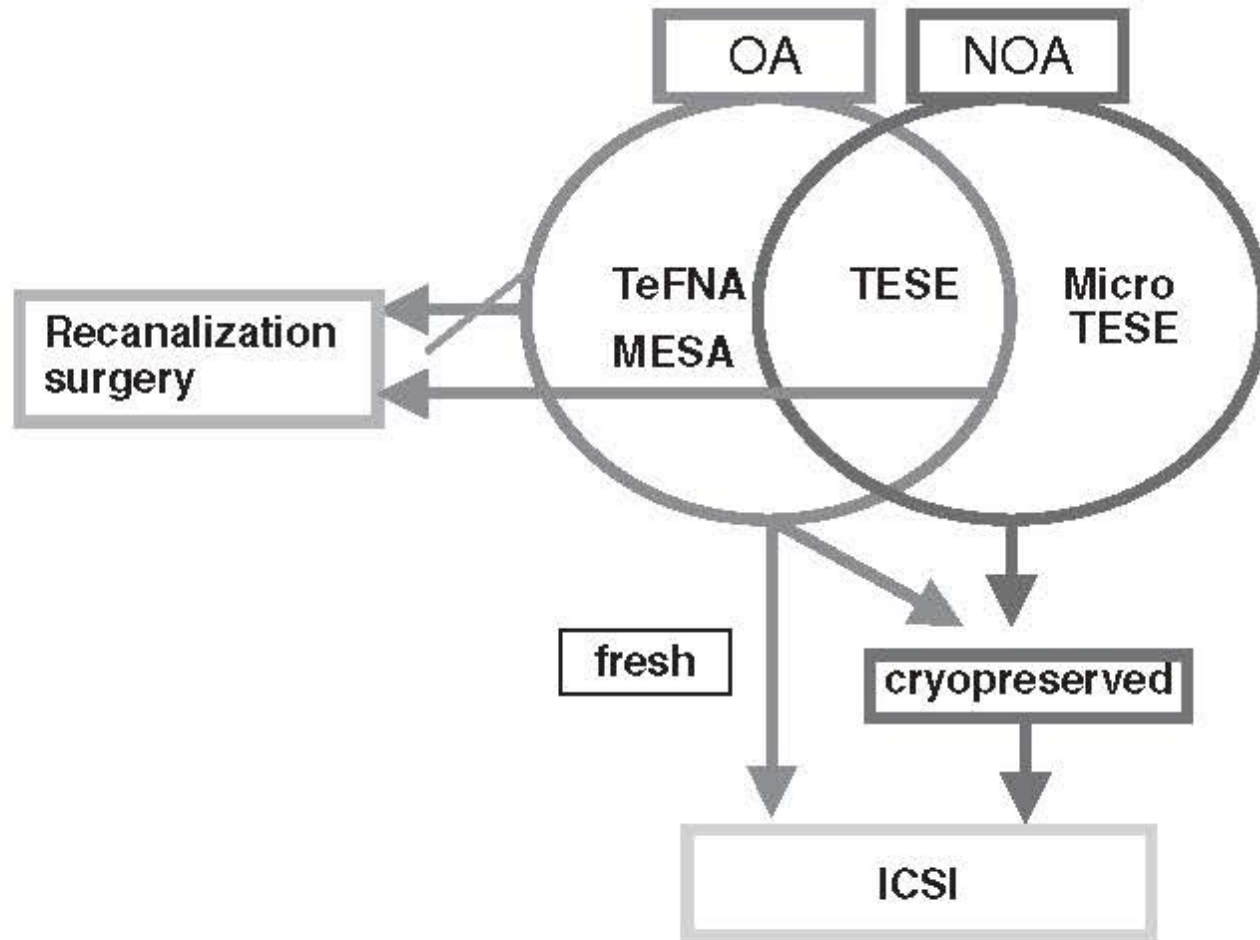
RECOMMENDATION

- ❖ For couples with RPL, men should be evaluated with **karyotype** (Expert Opinion) and sperm **DNA fragmentation**. (Moderate Recommendation; Evidence Level Grade: C)

SDF, Ejaculatory and Testicular Sperm



A flowchart for treatment of azoospermia





RECOMMENDATION

- ❖ Patients with **NOA should** be informed of the **limited** data supporting pharmacologic manipulation with SERMs, AIs, and gonadotropins prior to surgical intervention. (Conditional Recommendation; Evidence Level Grade: C)

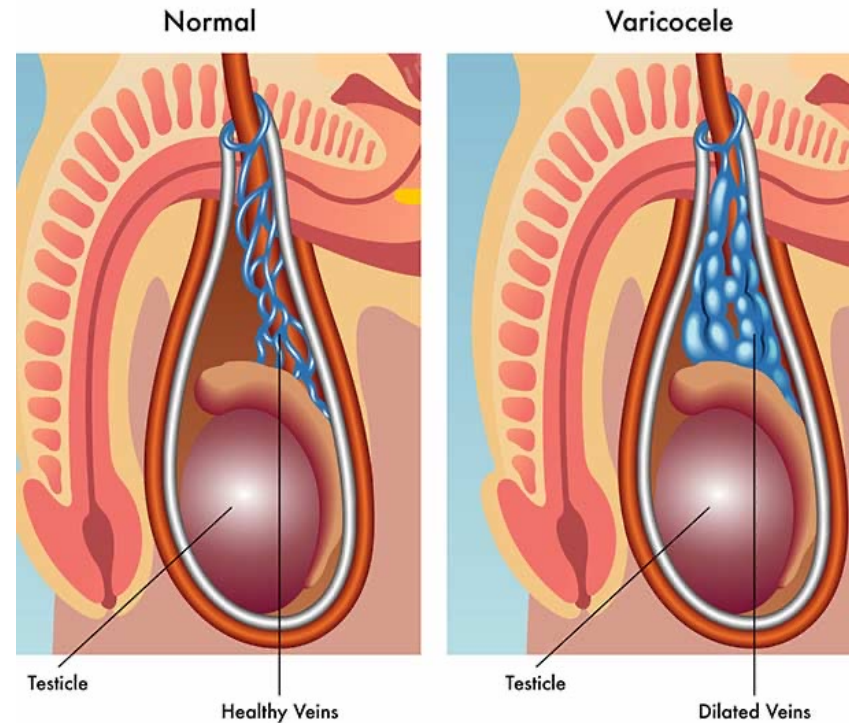


RECOMMENDATION

- For men with **NOA** undergoing sperm retrieval, **microdissection testicular sperm extraction (TESE)** should be performed. (Moderate Recommendation; Evidence Level: Grade C)
- In men undergoing surgical sperm retrieval, **either fresh or cryopreserved sperm** may be used for ICSI. (Moderate Recommendation; Evidence Level: Grade C)
- In men with azoospermia due to **obstruction** undergoing surgical sperm retrieval, sperm may be extracted from **either the testis or the epididymis**. (Moderate Recommendation; Evidence Level: Grade C)

Varicocelelectomy and its alternatives

The incidence of varicocele is **25.4%** in men with abnormal semen parameters and **11.7%** in men with normal semen parameters



- 15% of all men
- 35% of primarily infertile men
- 60-80% of secondarily infertile men
- Reason for infertility: ?hypoxia;hyperthermia?

Physical Examination: Varicocele

Subclinical	Not detected on physical exam; found by radiologic or other imaging study.
Grade I	Only palpable during or after Valsalva maneuver on physical exam
Grade II	Palpable on routine physical exam without Valsalva maneuver.
Grade III	Visible to the eye and palpable on physical exam.

Repair Clinical Varicocele Only

Varicocelectomy

- Multiple approaches have been developed for varicocele ligation:

- By Technique

- Conventional
- Microsurgical
- Laparoscopic
- Radiographic occlusion

A 2007 survey of 258 members of the American Urological Association performing varicocelectomy found that:

18% used an operating microscope,

48% used loupe magnification,

34% used no magnification, and 7% used the laparoscopic technique

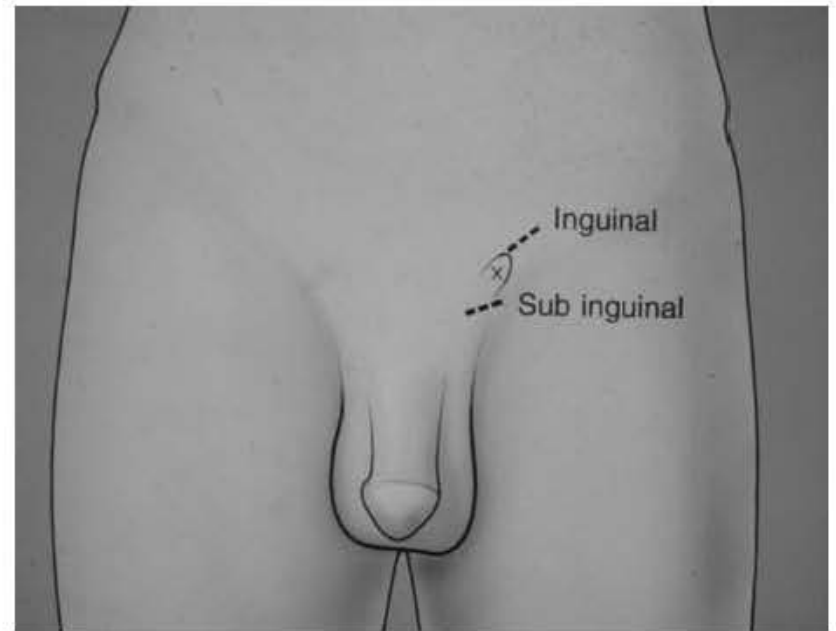
- By Anatomic Sites

- scrotal
- retroperitoneal
- inguinal
- subinguinal

Although the scrotal approach was one of the earliest employed, it is avoided nowadays, as injury to the testicular artery is more likely with a scrotal dissection.

Varicocelectomy

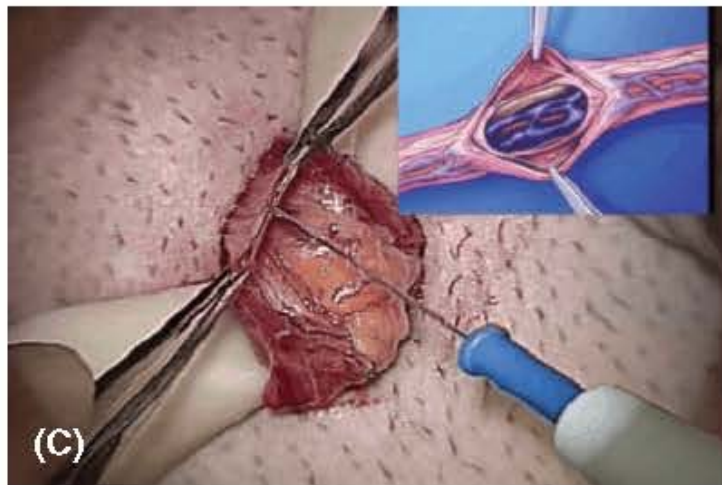
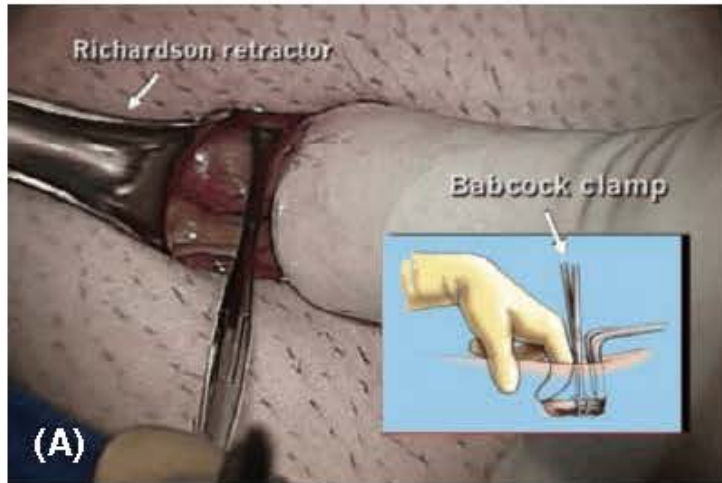
The location of the external inguinal ring is determined by invagination of the scrotal skin.



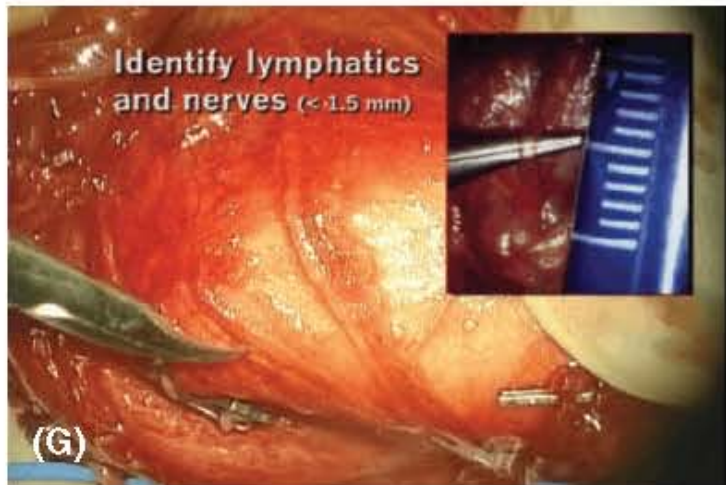
The subinguinal approach is preferable in men:

- with a history of prior inguinal surgery
- with obesity.
- with high, lax, capacious external rings
- with long cords and low-lying testes

Varicocelectomy (Inguinal/subinguinal)



Varicocelectomy (Inguinal/subinguinal)



Varicocelectomy Complications

- Hydrocele formation
 - <1% inguinal/subinguinal approach **with** microscope
 - UP 14% inguinal/subinguinal approach **without** microscope
 - 24% Retroperitoneal approach
- Testicular atrophy following artery ligation

The use of an **operating microscope** and **intraoperative Doppler** reduces the risk of inadvertent testicular artery injury.

Fertility improvement after Varicocelectomy

- The spontaneous pregnancy rate expected (in the absence of female factor)
 - 43% at one year
 - 69% at two years
- Madgar et al. randomized infertile men with abnormal semen parameters and varicocele to 2 groups:
 - surgery **immediately** or **one year** after the start
 - of the study.
 - Pregnancy rates were
 - **60%**, 12%, and 4% at one-, two-, and three-year follow-up, respectively.
 - In the delayed surgery group, spontaneous pregnancy rate during the first year without treatment was **11%**. Pregnancy rates at one- and two-year follow-up after delayed surgery were 44% and 22%, respectively.



RECOMMENDATION

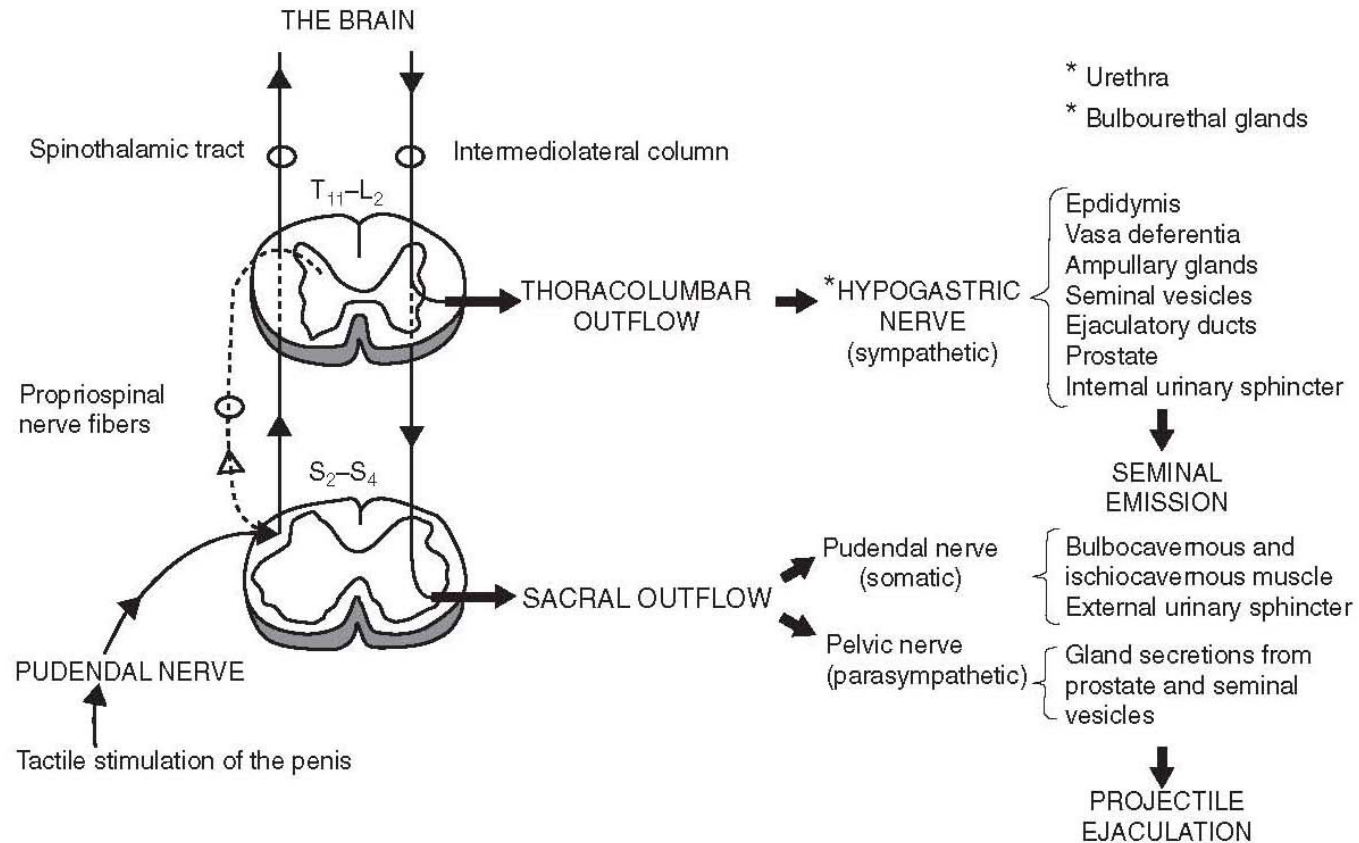
- **Surgical varicocelectomy** should be considered in men attempting to conceive who have **palpable varicocele(s), infertility, and abnormal semen parameters**, except for azoospermia men. (Moderate Recommendation; Evidence Level: Grade B)
- Clinicians should **not** recommend varicocelectomy for men with non-palpable varicoceles detected **solely by imaging**. (Strong Recommendation; Evidence Level: Grade C)
- For men with clinical **varicocele and NOA**, couples should be informed of the absence of definitive evidence supporting varicocele repair prior to ART (Expert Opinion)

Neurostimulatory methods to induce ejaculation

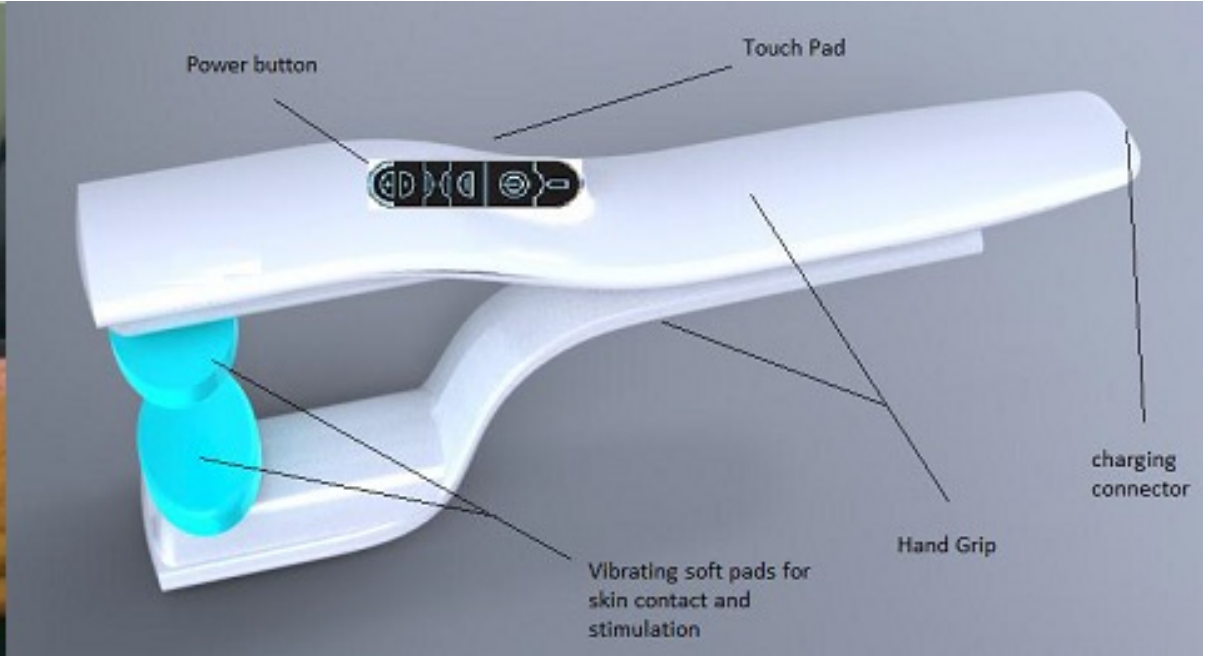
Indications

- Men with neurogenic anejaculation
 - Spinal Cord Injury
- Psychogenic anejaculation
- Diabetics anejaculation
- Age related anejaculation
 - Adolescent boys in risk of infertility
 - Cancer patients

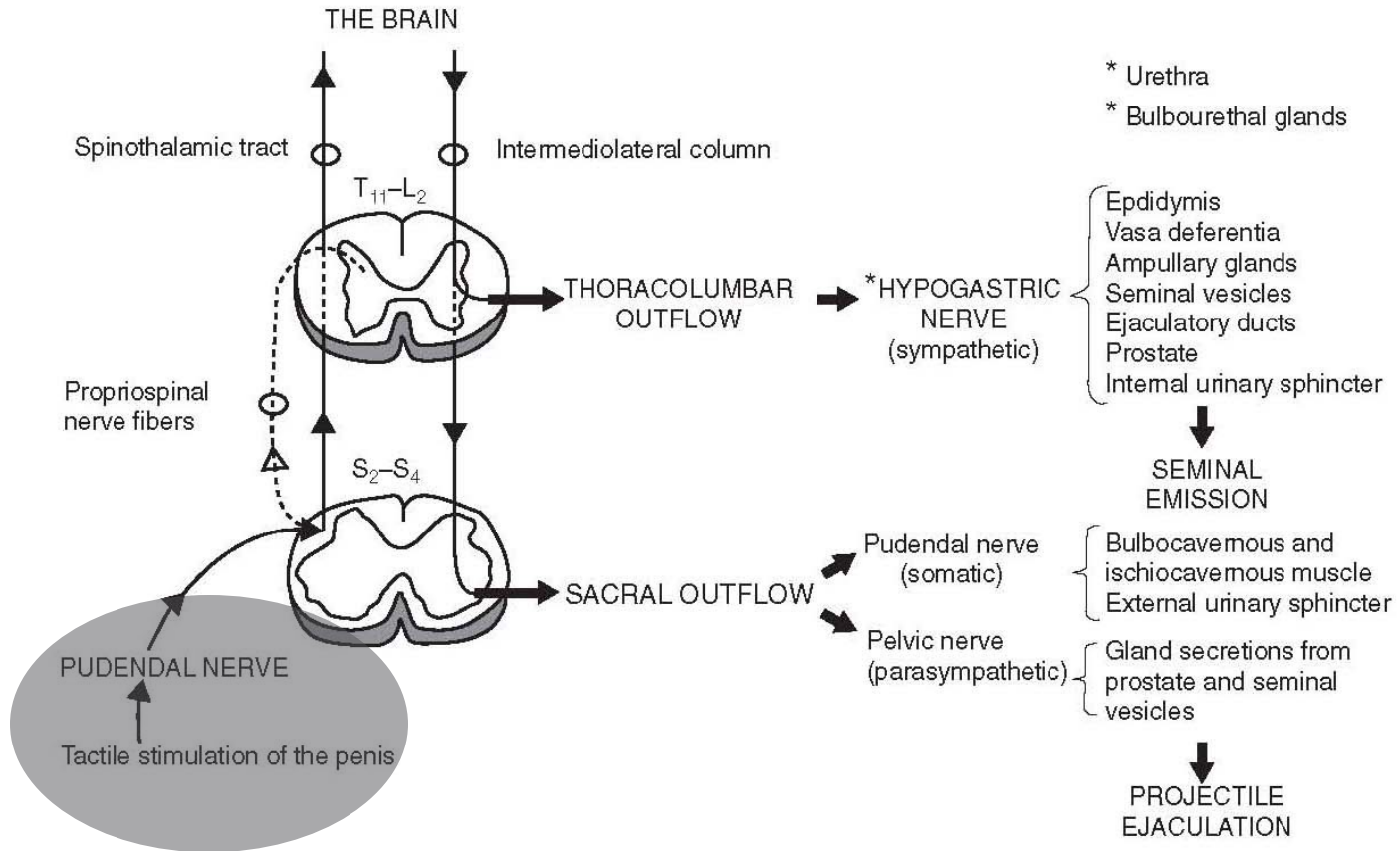
Spinal innervation of ejaculation



Penile Vibration Stimulation (PVS)

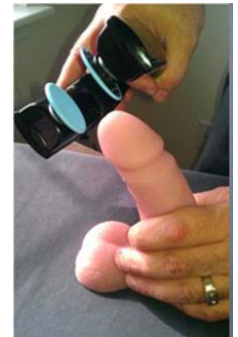


Spinal innervation of ejaculation



How to use?

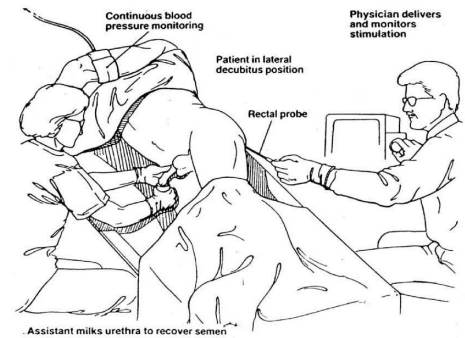
- Placing a vibrator on the glans penis
- Goal: recruiting the ejaculatory reflex to induce ejaculation
- Patients whose level of injury is T6 or rostral should be administered 20 mg nifedipine orally 30 minutes before PVS
- Supine position
- 2–5 min stimulation, interspersed by 1–2 min rest period (maximum 3 trials).
- Another person holds the semen collection container close to the urethral meatus



Penile Vibration Stimulation (PVS)

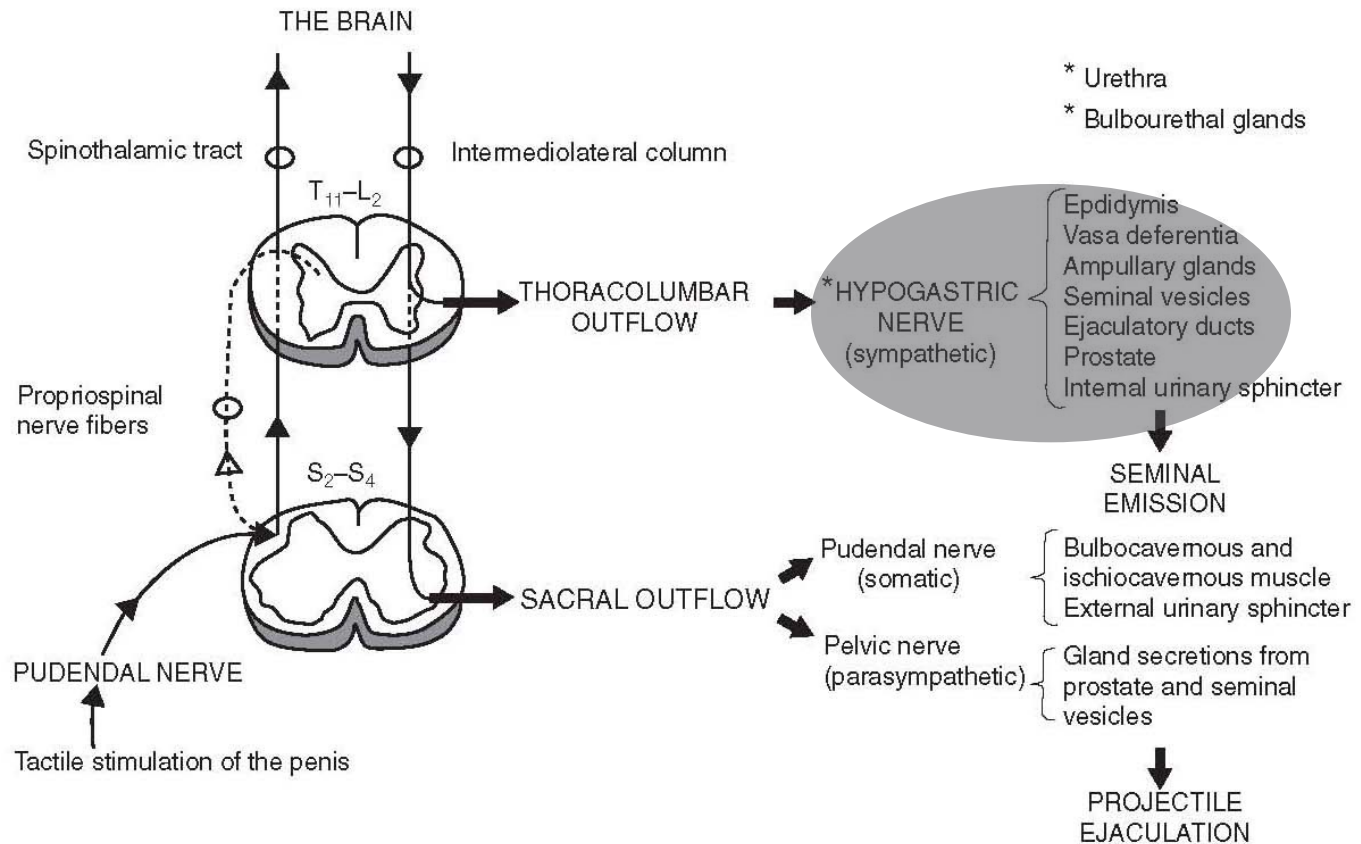


How to use?



- Placing a probe in the rectum
- Goal: electric stimulation toward prostate and seminal vesicles
- Patients whose level of injury is T6 or rostral should be administered 20 mg nifedipine orally 30 minutes before PVS
- Lateral decubitus position
- Anesthesia?
- Bladder Catheterization immediately before EEJ (remove the catheter)
- Rectoscopy prior to EEJ
- Wave-like pattern stimulation; 10-20 stimulations

Spinal innervation of ejaculation





RECOMMENDATION

- For men with **NOA** undergoing sperm retrieval, **microdissection testicular sperm extraction (TESE)** should be performed. (Moderate Recommendation; Evidence Level: Grade C)
- In men undergoing surgical sperm retrieval, **either fresh or cryopreserved sperm** may be used for ICSI. (Moderate Recommendation; Evidence Level: Grade C)
- In men with azoospermia due to **obstruction** undergoing surgical sperm retrieval, sperm may be extracted from **either the testis or the epididymis**. (Moderate Recommendation; Evidence Level: Grade C)

FUTURE SESSIONS

- ❖ **Session One:** Clinical investigation of the infertile male
- ❖ **Session Two:** Genetic causes of male infertility and their impact on future generations
- ❖ **Session Three:** Medical Treatments for Male Infertility
- ❖ **Session Four:** Surgical Treatments and Assisted Reproductive Technology (ART) for Male Infertility
- ❖ **Session Five:** Ejaculatory disorders
- ❖ **Session Six:** Clinical investigation and laboratory analyses in male hypogonadism
- ❖ **Session Seven:** Testosterone deficiency syndrome, , Androgen replacement—indications and principles
- ❖ **Session Eight:** Female-to-Male Transsexualism

