Evaluation and Treatment of the Subfertile Male

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Disclosures: None

Off label uses: There are no oral medications approved by the FDA for the treatment of male infertility
Why bother?
Intracytoplasmic sperm injection ICSI is...

• Not necessary for all couples
• Not financially feasible
• Not without risk
  • Multiples
  • Birth defects
  • Ovarian hyperstimulation syndrome
    • 1-3% severe OHSS
Male infertility is...

• Psychological burden
• Serious conditions
  • Cancer, genetic disorder, endocrinopathy, infection
• Treatable

• Goals:
  • Provide an overview of the evaluation and treatment options for the subfertile male

“You need to get your cholesterol where your sperm count is.”
Who is infertile?

• One in ten couples will struggle to obtain a pregnancy

• Fertile couples
  • 80% couples will conceive in 1st year
    • 15% per month
  • 10% in the 2nd year
Male evaluation

• History
  • Reproductive hx
  • PMHx
    • Cancer, childhood illness, chronic illness, puberty, GU infections, Traumatic brain injury, pelvic trauma
  • SHx
    • Pelvic, inguinal, genitourinary
  • FHx
    • Infertility, recurrent miscarriages, birth defects, cystic fibrosis
Male evaluation

• Medications
  • Testosterone, SSRI, antihypertensives, BPH

• Review of systems
  • Endocrinopathies
  • Genitourinary symptoms
Male evaluation

• Exposures
  • Illicit drugs, tobacco, heavy EtOH, heat, pesticides, petrochemicals

• Physical exam
  • Virilization, BMI, urethra meatus, testicles and scrotal contents

• Don’t take the physical exam for granted!
  • Vasa present?
Male evaluation

• Laboratory
  • Semen analysis x 2
  • Hormone screening
    • Fasting, morning blood draw
    • Total testosterone, LH, FSH, estradiol

• Genetic testing
• Urine testing
• Specialized semen testing

• Scrotal sonography
Categorizing patient by diagnosis

- Varicocele 38%
- Idiopathic 23%
- Obstruction 13%
- Normal 9%
- Cryptorchidism 3%
- Testicular failure 3%
- Antisperm antibodies 2%
- Gonadotoxin 2%
- Endocrinopathy 1%
- Pyospermia 1%
- Genetic 0.5%
- Torsion 0.5%
- Erectile dysfunction 0.4%
- Testis cancer 0.4%
Treatment

Medical

Surgical

ART
Hypothalamic pituitary gonadal axis

• Promotes androgen synthesis and spermatogenesis

• Feedback and feed forward mechanisms

• Medical therapies for male infertility aim to correct or influence HPG axis
Medical therapies

- hCG
  - LH, FSH analog
  - Hypogonadotropin hypogonadism

- Clomiphene
  - Estrogen receptor blocker

- Anastrozole
  - Aromatase inhibitor
Medical therapies

• Not testosterone!
  • Exogenous testosterone suppresses sperm production
Medical therapies - Ejaculatory dysfunction

- Premature ejaculation
  - SSRIs, topical anesthetic, counseling

- Retrograde ejaculation
  - Sympathomimetics

- Anejaculation / anemission
  - Stop psych meds
  - Stop BPH meds
  - Trial sympathomimetics

- Erectile dysfunction
  - PDE-5, intraurethral alprostadil, ICI
Surgical Treatment
Surgical Treatment: Varicocelectomy

• Varicocele
  • 15% of men
  • 40% men in infertile couples
    • 80% men with secondary infertility
  • Majority are left sided
Varicocele

• Impaired semen parameters
  • Decreased count, motility, and % nl morphology
  • Increase DNA fragmentation and ROS
Varicocelectomy

• Subinguinal microsurgical varicocelectomy
  • Dilated veins ligated
  • Vas deferens, artery, lymphatics, normal sized veins spared
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Varicocelectomy outcomes

• Majority of men will have improvement in semen parameters
  • Concentration
  • Motility
  • Progressive motility
  • % nl morphology
  • % intact DNA
  • Decreased seminal ROS

• Increase chance of spontaneous pregnancy....
  • Increased pregnancy in oligospermic couples OR 2\(^1\) to 2.8\(^2\)

\(^1\)Cochrane Review 2009, \(^2\)Marmar 2007
Varicocelectomy outcomes

Couples benefit from varicocelectomy

....but not every couple benefits from varicocelectomy
Surgical Treatment: Vasal reconstruction

• Vasectomy

• Iatrogenic injury
  • Hydrocele, orchidopexy, hernia repair

• Infection
Surgical Treatment: Vasal reconstruction

• Vasovasostomy
  • Formal 2 layer
    • 10-0 nylon mucosa
    • 9-0 nylon muscle + adventitia
  • Modified 2 layer
    • 9-0 “full thickness” mucosa, muscle adventitia
    • 9-0 “tweener” muscle + adventitia
Surgical Treatment: Vasal reconstruction

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- Comparable outcomes
- Modified 2 layer is cheaper
Surgical Treatment: Vasal reconstruction

• Absence of effluent from testicular vas?
• Absence of sperm parts in effluent?

→ Proceed to vasoepididymostomy
Surgical Treatment: Vasoepididymostomy

• Longitudinal intussusception vasoepididymostomy
  • Vas is mobilized
    • 6-0 prolene vas adventitia to secure in proximity to epididymis
  • Candidate epididymal tubule selected
  • 10-0 nylon needles passed into epididymal tubule
    • Parallel to long axis
  • Incise tubule and examine effluent
  • 10-0 needles passed through mucosa +/- muscle of vas
  • 9-0 nylon pex vas adventitia to epididymal tunica
Surgical Treatment: Vasoepididymostomy

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- Tension free, water tight anastomosis
Vasal Reconstruction: Outcomes

- VV
  - Patency 90% (92.8%)
  - Pregnancy 60-70%
    - Age of the spouse most important determinate

- VE
  - Patency 60-70%
  - Pregnancy 20-40%
    - Maturation defect in sperm
ART: Spontaneous Conception

Trial of timed intercourse (TCC)

Maximize the chance of an egg encountering a sperm
ART: Timed intercourse

- Sperm = 3+ days
- Egg = 12 to 24 hour

Intercourse every other day beginning day 10 and continuing for 1 week
ART: Intrauterine insemination (IUI)

- 10 million motile sperm pre-wash
- 3ml 9M/ml 45% = 12.15 million motile sperm
- 15% pregnancy / cycle = on par with natural conception
ART: In-vitro fertilization

~ 100,000 motile sperm
ART: Intracytoplasmic sperm injection

IVF

~ 100,000 motile sperm

ICSI

~ 10,000 motile sperm
Surgical Treatment: Sperm Retrieval
Sperm Aspiration: PESA

• Percutaneous epididymal sperm aspiration
  • Light sedation or local anesthetic
  • 90% SR
  • <10% complication
  • Short recovery
Sperm aspiration: TESA

• **Testicular sperm aspiration**
  • Anesthetic depends on technique
    • FNA
    • True cut needle
    • Needle gun (ouch!)
  • Sperm retrieval rate depends on histology
  • Complications vary
    • <10%
  • Short recovery
  • Tissue is more labor intense for embryologist
Sperm retrieval: TESE and MTESE

• Conventional
  • Random sampling of tubules

• Microsurgical
  • Optical magnification
  • Directed sampling based on appearance of tubules
  • Thorough assessment entire testis
MTESE vs TESE- outcomes

• MTESE superior to convention TESE
  • Sperm found in 50% men MTESE
    • 15-30% conventional TESE
MTESE vs TESE- outcomes

• Histology predicts success
  • Hypospermatogenesis: 80 - 90%
  • Maturation arrest: 47-75%
  • Germ cell aplasia / Sertoli cell only syndrome: 16 -33.9%

• Genetics predict success
  • AZFc, XXY

• High FSH, low testosterone, small testis size do not preclude finding sperm
Summary

• Male fertility evaluation is valuable

• Standard tests are adequate for many couples
Summary

• Targeted therapy may
  • Correct male factor
  • Expand treatment options
  • Improve outcomes of ART

• Results guide couples towards best treatment options
Questions