



EVALUATION OF MALE INFERTILITY

FLAME LECTURE: 222B

PERCIVAL/BURNS 9.9.15

Learning Objectives

- ▶ Define infertility
- ▶ Describe causes of male and female infertility
- ▶ Describe the evaluation of an infertile couple
- ▶ List the psychosocial issues associated with infertility
- ▶ Prerequisites:
 - ▶ FLAME LECTURES: 213A-B – Menstrual Cycle and Ovulation
- ▶ See also – for closely related topics
 - ▶ FLAME LECTURE 222A – Evaluation of Female Infertility
 - ▶ FLAME LECTURE 222C – Management of Infertility
 - ▶ FLAME LECTURES: 208-209 – Evaluation & Treatment of PCOS

Etiology of Infertility

- ▶ Approximately 8-15% of couples are unable to conceive after 1 year of unprotected intercourse
- ▶ **Primary infertility**: a woman has **never** been able to get pregnant
- ▶ **Secondary infertility**: a woman has been pregnant in the past, but has 1 year of inability to conceive
- ▶ **Fecundability**: the probability of achieving a pregnancy within one menstrual cycle = 20-25%
 - ▶ After 12 months, 85% of couples should conceive
 - ▶ Varies significantly by maternal age

Etiology of Infertility

- ▶ Evaluation is warranted after 1 yr of trying for women <35 yo and after 6 months of trying for women > 35 yo
- ▶ Earlier evaluation may also be justified based on medical history and physical findings:
 - ▶ Oligomenorrhea or amenorrhea
 - ▶ Known or suspected uterine/tubal/peritoneal disease or severe endometriosis
 - ▶ Known or suspected male subfertility

Causes of Infertility	
Male Factor	26%
Ovulatory Dysfunction	21%
Tubal Damage	14%
Endometriosis	6%
Coital Problems	6%
Cervical Factors	3%
Unexplained	28%

Evaluation of Infertile Male - *History*

- ▶ **Sexual History:**
 - ▶ Coital frequency & timing
 - ▶ Duration of infertility & previous fertility
 - ▶ History of STI's
 - ▶ Difficulty with erection or ejaculation
- ▶ **Past Medical/Surgical history:**
 - ▶ Childhood illnesses & developmental hx
 - ▶ Systemic medical illnesses (i.e. Diabetes)
 - ▶ Hx of hernia/varicocele +/- repair, Mumps
- ▶ **Social history:**
 - ▶ Caffeine, alcohol intake, smoking, illicit drug use, toxic exposures at work, heat exposures (frequent hot tub?)
- ▶ **Family history:** infertility, cancer, developmental delay, birth defects
- ▶ **Medications:** Anabolic steroid use

Evaluation of Infertile Male - *Physical*

- ▶ Detailed exam not required if semen analysis is normal
- ▶ If semen analysis abnormal, refer to Urology for:
 - ▶ Examination of penis and location of urethral meatus
 - ▶ Palpation and measurement of testes
 - ▶ Presence and consistency of vas deference and epididymides
 - ▶ Presence or absence of varicocele
 - ▶ Secondary sexual characteristics (body habitus, hair distribution, breast development)
 - ▶ Digital rectal exam when indicated

Evaluation of Infertile Male – *Semen Analysis*

- ▶ Cornerstone of laboratory evaluation
- ▶ Pre-test abstinence interval (2-5 days)
- ▶ If collected at home, specimen should be kept at room or body temp during transport and delivered to lab within 30 mins to 1 hour
- ▶ Evaluates volume, concentration, motility, & morphology

Evaluation of Infertile Male – *Semen Analysis*

- ▶ Normal measures for predicting fertilization capacity:
 - ▶ Volume of ejaculate: ≥ 1.5 mL
 - ▶ Total sperm in ejaculate: ≥ 39 million
 - ▶ Concentration: ≥ 15 million/mL
 - ▶ Motility: $\geq 40\%$
 - ▶ Morphology (Kruger strict criteria): $\geq 4\%$
- ▶ If any measures are equivocal, consider repeating the analysis keeping in mind that every three months the entire sperm population will have turned over

Evaluation of Infertile Male – *Endocrine Evaluation*

- ▶ Uncommon cause of male infertility
- ▶ Endocrine evaluation indicated for:
 - ▶ Sperm concentration < 10 million/mL
 - ▶ Impaired sexual function
 - ▶ Other clinical findings suggestive of a specific endocrinopathy
- ▶ Testing:
 - ▶ If total Testosterone < 300 ng/mL, consider free T & LH to evaluate for hypogonadism or exogenous steroid use
 - ▶ Prolactin/TSH if concerned for pituitary adenoma

Evaluation of Infertile Male – *Ultrasound*

▶ **Transrectal ultrasound**

- ▶ May help with dx of ejaculatory duct obstruction (dilated seminal vesicles, midline prostatic cysts, etc.)

▶ **Scrotal ultrasound**

- ▶ May identify small varicoceles, but these may not be clinically significant
- ▶ May help with vague/ambiguous physical findings (masses, small scrotal sac, etc.)
- ▶ Should be considered if risk factors for testicular cancer present (cryptorchidism, previous testicular neoplasm, etc.)

Evaluation of Infertile Male – *Other Lab Tests*

LAB TESTS TO EVALUATE CAUSES OF MALE INFERTILITY

Post-ejaculatory Urinalysis

- Consider a post-ejaculate urinalysis in men having ejac volume <1 mL (except in those with hypogonadism or CBAVD, incomplete collection, or very short abstinence interval)
- Low volume or absent anterograde ejaculate suggests
 - incomplete collection
 - retrograde ejaculation
 - lack of emission
 - ejaculatory duct obstruction
 - hypogonadism
 - congenital bilateral absence of vas deferens (CBAVD)
- Examine urine for sperm

Leukocytes in Semen

- For true pyospermia (>1 million leukocytes/mL), evaluate for genital tract infection or inflammation
- Leukocytes in sperm can both damage sperm themselves, or be correlated with condition contributing to infertility
- Treat leukospermia with 10-day erythromycin or TMP/SMX
 - Not often successful at relieving infertility even if leukospermia resolves
 - Gonorrhea, pelvic TB, other STI's can lead to epididymis/VD obstruction

Evaluation of Infertile Male – *Other Lab Tests continued*

LAB TESTS TO EVALUATE CAUSES OF MALE INFERTILITY

Anti-Sperm Antibodies

- Normally sperm are protected from autoimmune attack
- Rare cause of male subfertility
 - Can be treated with up to 6 months of glucocorticoids
- Clinical utility of testing is uncertain
- Unnecessary if IVF with ICSI planned - Routine testing NOT indicated

Sperm DNA Fragmentation Tests

- Testing analyzes the number of breaks in the sperm DNA or looks for abnormal chromatin structure
- Not enough evidence to support routine testing

Evaluation of Infertile Male – *Genetic Screening*

- ▶ Should be considered in men with non-obstructive azoospermia or severe oligospermia (<5 million/mL)
- ▶ Cystic Fibrosis gene mutations
 - ▶ Strong association between CBAVD and mutations in CFTR gene
 - ▶ 80% of men with CBAVD have documented mutations in the CFTR gene
 - ▶ Should also test female partner of affected men
- ▶ Karyotypic chromosomal abnormalities
 - ▶ Present in 10-15% of azoospermic men, 5% in men with severe oligospermia
 - ▶ Klinefelter syndrome (47,XXY) accounts for 2/3 of chromosomal abnormalities in infertile men
- ▶ Y-chromosome micro-deletions
 - ▶ 16% of men with azoospermia or severe oligospermia
 - ▶ Sons of individuals with Y-chrom microdeletion will inherit the abnormality

SUMMARY OF FIRST STEPS

- ▶ Take a thorough History & PE
- ▶ Begin with the least invasive testing:
 - ▶ **Ovulatory factor:**
 - ▶ Menstrual history and history of positive OPKs?
 - ▶ Cycle Day 3 FSH, E2
 - ▶ Baseline Antral Follicle Count and serum AMH
 - ▶ Serum Prolactin and TSH
 - ▶ **Tubal and Uterine Factor:**
 - ▶ TVUS to evaluate for non-cavity uterine pathology (ex. fibroids)
 - ▶ Hysterosalpingogram to evaluate uterine cavity and tubal patency
 - ▶ **Male Factor:**
 - ▶ Semen analysis
 - ▶ **STI testing** is required in most states for males and females before fertility treatments may begin

IMPORTANT LINKS / REFERENCES



- ▶ Uptodate – Causes of Male Infertility
- ▶ Uptodate – Evaluation of Male Infertility
- ▶ <http://www.acog.org/About-ACOG/ACOG-Departments/Patient-Safety-and-Quality-Improvement/How-I-Practice/Infertility-Workup>