Evaluation of Male Infertility:

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Definition of Infertility:

Lack of conception after 1 year of unprotected intercourse
Epidemiology of Infertility:

• Affects 10% to 15% of couples.

• Male factor can be identified in 50% of these cases.
Male Infertility: Categories:

Divided into 4 categories

• Pre-testicular
• Testicular
• Post-testicular
• Idiopathic.
History:
Vital Questions:

• Time the couple has been engaging in unprotected intercourse.

• Frequency and timing of intercourse with respect to the female partner’s menstrual cycle.

• Primary or secondary Infertility.
History:
Medical Conditions:

• Systemic inflammation due to chronic conditions.

• Neuropathic conditions.

• Endocrine Abnormalities.
History:
Medications:

- Anabolic steroids, exogenous testosterone.
- $5^\alpha$ reductase inhibitors.
- Other drugs...
History:
Infection/Inflammation:

- Fever $\rightarrow$ suppressive effect on spermatogenesis.

- A history urethritis $\rightarrow$ obstructive causes of male factor infertility.

- Mumps!

- Recurrent sinus infections or bronchitis $\rightarrow$ immotile cilia syndrome.
History:

Prior Surgery:

- A history of pediatric hernia repair, orchiopexy or other scrotal surgery.

- Adult Herniorrhaphy… rarely!

- Orchiectomy for torsion or cancer.

- TURP.
Physical Examination:

• Secondary sex characteristics.
• Phallus.
• Testes.
• Epididymis.
• Spermatic cord.
Laboratory Testing: Semen Analysis

• Most important laboratory component of the evaluation.

• At least 2 adequate semen analyses are required.

• Significant day-to-day variation in many semen parameters.
# Laboratory Testing: Semen Analysis

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Volume (mL)</td>
<td>ND</td>
<td>≥ 2</td>
<td>≥ 2</td>
<td>≥ 2</td>
<td>1.5</td>
</tr>
<tr>
<td>Sperm count (10⁶/mL)</td>
<td>20-200</td>
<td>≥ 20</td>
<td>≥ 20</td>
<td>≥ 20</td>
<td>15</td>
</tr>
<tr>
<td>Total sperm count (10⁶)</td>
<td>ND</td>
<td>≥ 40</td>
<td>≥ 40</td>
<td>≥ 40</td>
<td>39</td>
</tr>
<tr>
<td>Total motility (% motile)</td>
<td>≥ 60</td>
<td>≥ 50</td>
<td>≥ 50</td>
<td>≥ 50</td>
<td>40</td>
</tr>
<tr>
<td>Progressive motility²</td>
<td>≥ 2³</td>
<td>≥ 25%</td>
<td>≥ 25% (grade a)</td>
<td>≥ 25% (grade a)</td>
<td>32% (a + b)</td>
</tr>
<tr>
<td>Vitality (% alive)</td>
<td>ND</td>
<td>≥ 50</td>
<td>≥ 75</td>
<td>≥ 75</td>
<td>58</td>
</tr>
<tr>
<td>Morphology (% normal forms)</td>
<td>80.5</td>
<td>≥ 50</td>
<td>≥ 30⁴</td>
<td>(14)⁵</td>
<td>4⁶</td>
</tr>
<tr>
<td>Leukocyte count (10⁶/mL)</td>
<td>&lt; 4.7</td>
<td>&lt; 1.0</td>
<td>&lt; 1.0</td>
<td>&lt; 1.0</td>
<td>&lt; 1.0</td>
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</tbody>
</table>

¹ Reference: [WHO 2010 Guidelines for the Evaluation of the Male Fertility](https://www.who.int/publications/i/item/9789241548123)

² Progressive motility refers to the percentage of sperm that exhibit progressive forward movement.

³ Sperm concentration is calculated by dividing the number of sperm per milliliter by the volume of semen.

⁴ Morphology refers to the visual assessment of sperm shape and size.

⁵ The percentage of morphologically normal sperm is a key parameter in semen analysis.

⁶ The number of leukocytes in semen is important as an indicator of semen quality.
Laboratory Testing: 
Semen Analysis

• Volume: important determinant of absolute sperm number, sufficient quantity of alkaline buffers.

• Concentration: most critical determinant of fertility potential.

• Motility: assessment of the movement capacity of sperm
# Laboratory Testing: Semen Analysis

## APPENDIX 1: DIFFERENTIAL DIAGNOSIS OF COMMON SEMEN ABNORMALITIES

<table>
<thead>
<tr>
<th>Semen Analysis Result</th>
<th>Differential Diagnosis</th>
</tr>
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<tbody>
<tr>
<td>Low volume</td>
<td>Specimen error, medications, congenital bilateral absence of vas deferens, hypogonadism, retrograde ejaculation, anejaculation, ejaculatory duct obstruction</td>
</tr>
<tr>
<td>Low count or concentration</td>
<td>Genetic, environmental exposure, heat exposure, varicocele, chemotherapy, radiation therapy, vasectomy or surgical obstruction of reproductive tract, infection (mumps or severe epididymo-orchitis), cryptorchidism</td>
</tr>
<tr>
<td>Low motility</td>
<td>Varicocele, genetic, environmental exposure, heat exposure, varicocele, chemotherapy, radiation therapy</td>
</tr>
</tbody>
</table>
Laboratory Testing: 
Semen Analysis

• Morphology: unclear significance except in cases of IVF

• Only 4% normal forms by Kruger criteria are likely to initiate fertilization.

• Cause for alarm in many patients ➔ Reassurance.
Laboratory Testing: Semen Analysis

- Semen pH: indicator of seminal vesicle patency.
- Fructose: diagnosis of seminal vesicle obstruction or agenesis.
- Lower pH and fructose levels may reflect obstruction of the ejaculatory duct.
Laboratory Testing: Semen Analysis

• Semen viscosity: prognostic significance of high semen viscosity is unclear.

• Round cells in semen: leukocytes or immature spermatogonia.
Laboratory Testing: Serum testing

• 10% of infertile men have abnormal serum hormone levels.

• Hormonal testing is indicated for men with severe oligospermia or azoospermia.

• The minimum hormonal evaluation includes serum testosterone and FSH.
### APPENDIX 2: HORMONE PARAMETERS IN VARIOUS FERTILITY STATES

<table>
<thead>
<tr>
<th></th>
<th>Testosterone</th>
<th>LH</th>
<th>FSH</th>
<th>Prolactin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Primary testis failure</td>
<td>Low</td>
<td>High</td>
<td>High/normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Secondary testis failure (hypogonadotropic hypogonadism)</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
<td>Normal</td>
</tr>
<tr>
<td>Hyperprolactinemia</td>
<td>Low</td>
<td>Low/normal</td>
<td>Low</td>
<td>High</td>
</tr>
<tr>
<td>Androgen resistance</td>
<td>High</td>
<td>High</td>
<td>High</td>
<td>Normal</td>
</tr>
</tbody>
</table>
Laboratory Testing: Genetic testing

• Prevalence of genetic abnormalities in infertile men is around 5%.

• Men with azoospermia or severe oligospermia are more likely to have diagnosable genetic abnormalities.

• Karyotype, screening for CFTR gene mutations...
Laboratory Testing: Genetic testing

- Y chromosome microdeletion assay: deletions in the portion of the Y chromosome critical for spermatogenesis.

- Abnormalities in the 3 regions of AZFa, AZFb and AZFc.
Laboratory Testing: Genetic testing

Figure 1 - Gene regions and markers currently known on the Y-chromosome.
Laboratory Testing: Antisperm antibody testing

- Antisperm antibodies may adhere to spermatozoa and impair their motility and/or lead to their destruction by immune cells.

- It is unclear how antisperm antibodies develop.

- Test ordered when there is prominent sperm agglutination and idiopathic asthenospermia.
Laboratory Testing:
Sperm-DNA fragmentation testing

• Measure of the quality of genetic material within sperm cells.

• high DNA fragmentation has been associated with impaired sperm motility and increased seminal oxidative stress.
Laboratory Testing: Sperm-DNA fragmentation testing
Laboratory Testing: Scrotal ultrasound

- Useful when the testicles are difficult to locate.
- Doppler ultrasound may be used to characterize varicoceles
Laboratory Testing: Transrectal Ultrasound

- Confirm presence of a midline cyst obstructing the ejaculatory duct
- Demonstrate dilatation or absence of the seminal vesicles.
Laboratory Testing: Testis biopsy and scrotal exploration

- Biopsy of the testis is indicated for the evaluation of azoospermia.

- Performed to verify if spermatogenesis is normal or impaired.
Conclusions:

The fundamental purpose of evaluating a man with fertility concerns:

• Estimation of the probability of conception with natural intercourse
• Identification of reversible factors
• Detection of occult but potentially serious comorbid or contributing medical conditions
• Detection of genetic variables that may impact the health and well-being of any offspring.
Conclusions:

Basic evaluation of the infertile man:

• Thorough history

• Physical examination

• The minimum laboratory evaluation includes 2 semen analyses, morning testosterone level and serum FSH.

• Additional testing may be useful as indicated by results of the basic evaluation
Thank You For Your Attention!

Some day I’m going to be an astronaut!

Well, there’s a good chance a bunch of us might be headed for Uranus!