Male infertility

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Outcomes

• Explain and integrate the cornerstones of male infertility evaluation
• Interpret the components of a standard spermiogram
• Classify the causes of male infertility and how you will come to a diagnosis
• Discuss the endocrine and genetic evaluation
• Discuss the management of male infertility
MALE REPRODUCTIVE ORGANS

• External genital organs
  – Penis
  – Scrotum
• Internal genital organs
  – Epididymis
  – Vas deferens
  – Testes
  – Accessory glands
    • Seminal vesicles
    • Prostate gland
    • Bulbourethral glands
HPG axis

- The **hypothalamic-pituitary-gonadal axis (HPG axis)** refers to the effects of the hypothalamus, pituitary gland, and gonads as a single entity.

- HPG axis plays a critical part in the development and regulation of a number of the body's systems:
  - Reproductive
  - Immune

- Fluctuations in the hormones cause changes in the hormones produced by each gland:
  - Having widespread and local effects on the body
HPG axis

• This axis controls
  – Development
  – Reproduction
  – Aging

• The hypothalamus produces
  – Gonadotropin-releasing hormone (GnRH)

• The anterior portion of the pituitary gland produces
  – Luteinizing hormone (LH)
  – Follicle stimulating hormone (FSH)

• The gonads produce
  – Estrogen
  – Testosterone
HPG axis

In the hypothalamus

- Gonadotropin releasing hormone (GnRH) is secreted from the GnRH neurons into the portal blood system
HPG-axis

In the pituitary

- GnRH receptors bind GnRH which induces the production and secretion of gonadotropins
  - Luteinizing hormone (LH)
  - Follicle stimulating hormone (FSH)

- LH and FSH travel systematically to the ovary (females) or testis (males) to induce the production of steroid hormones
In the testis:

- LH binds receptors on the Leydig cells which secrete testosterone in a paracrine manner to the Sertoli cells.
- Testosterone, DHT and/or estradiol negatively feed back from the testis to the hypothalamus and pituitary to regulate secretion of GnRH and LH.
- FSH binds to receptors on the Sertoli cells stimulating them to produce inhibin B, also secreted from the granulosa cells and feeds back negatively to the pituitary to regulate the secretion of FSH.
CAUSES OF MALE INFERTILITY

- Pre-testicular
- Testicular
- Post-testicular
Causes – Pre-testicular

• General factors
  – Viral illness, stress, age, nutrition, alcohol smoking etc

• Endocrine
  – Hypothalamic (Kallman’s syndrome), pituitary, adrenal, thyroid, Klinefelter’s (47xxy)

• Drugs
  – H$_2$ receptor antagonists, anabolic steroids, etc

• Chemotherapy

• Environmental toxins
Causes - Testicular

- Varicocele
- Undescended testes
- Previous testicular torsion/trauma
- Mumps orchitis
- Radiotherapy
- Previous surgery (inguinal hernia repair)
Causes – Post-testicular

- Congenital bilateral absence of the vas deferens
- Acquired ductal obstruction (eg previous epididymitis)
- Retrograde ejaculation (eg previous bladder neck surgery)
- Sexual problems
  - Premature ejaculation
  - ED
  - Penile problems (Peyronie’s disease, hypospadias)
- Inflammatory conditions (eg chronic prostatitis)
Human Infertility

Female 60%

Male 40%

10-15% of population
Male infertility

• ±15% of couples
• after one year regular, unprotected intercourse

• male factor
  – solely responsible ~ 20%
  – contributory ~30-40%

Male infertility factor: abnormal semen analysis
EVALUATION: INFERTILE MALE

- Special investigations
- History
- Physical Examination
WHEN to start evaluation

• after one year of regular unprotected intercourse

• evaluation before one year if
  – male infertility risk (history of bilateral UDT)
  – female infertility risk factors (female age >35 yrs)
  – questions about the male partner’s fertility
WHO should do evaluation?

• Initial screening by GP
  – abnormal male reproductive history
  – abnormal semen analysis

Refer to urologist/ male reproduction specialist
AIMS of evaluation

• potentially correctable conditions – eg life style factors
• irreversible conditions amenable - ART using partner sperm
• irreversible conditions for donor insemination or adoption (eg, azoospermia, immotile cilia syndrome)

- **life- or health-threatening conditions** that may underlie the infertility and require medical attention

• genetic abnormalities that may affect the **health of offspring** if ART are to be employed.
AIMS of evaluation

• detection of conditions for which there is no treatment will spare couples the distress of attempting ineffective therapies

• may allow the couple to better understand the basis of their infertility and to obtain genetic counseling when appropriate
Required evaluation every patient

1. History

1.1 Reproductive

- coital frequency and timing
- duration and prior fertility
- childhood illnesses, developmental history
- systemic medical diseases (diabetes mellitus, upper respiratory tract)
- sexual history, STD, HIV
- gonadal toxin exposure, eg heat
Required evaluation every patient

1.2  **Medical history**

- identify risk factors and behavior patterns that could have a significant impact on male infertility.
  - complete medical and surgical history
  - medications (prescription and OTC)
  - review of systems
  - family reproductive history
  - past infections: STD, URTI
  - spouse
Required evaluation every patient

2. **Physical examination**
   • Full clinical examination with particular focus:
     – testes size and consistency
     – penis and urethral meatus
     – presence/consistency both vasa and epididymides
     – varicocele
     – secondary sex characteristics including hair distribution and breast development
     – Digital rectal exam (DRE)
Required evaluation every patient

3. **Semen analysis**

- cornerstone laboratory evaluation & helps to define the severity of the male factor

- methods of semen analysis: WHO

- accredited laboratory, trained technologist
Semen analysis

- Semen analysis can be informative about problems in the male
  - Sperm production
  - Sperm transport and maturation
  - Sperm transfer and function in the female tract
Semen analysis (WHO)

• **Standard instructions for semen collection:**
  
  • defined abstinence 3 days
  • masturbation, special collection condoms
  • collected at the laboratory
  • evaluated within one hour of collection
  • Quality Control Programme
  • expert technologist
Semen analysis (WHO)

- volume
- count
- motility
- morphology

EXCLUDE ARTEFACTS as possible causes of abnormal semen parameters
Semen = “hazardous”

- Contain harmful infectious agents
  - HIV
  - Hepatitis
  - Herpes simplex
## WHO (1999/2010): reference values semen analysis

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<th>WHO 1999</th>
<th>ESHRE</th>
<th>WHO 2010</th>
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<tbody>
<tr>
<td><strong>pH</strong></td>
<td>7.2 or more</td>
<td>7.2 or more</td>
<td>&gt; 7.2</td>
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<tr>
<td><strong>Ejaculate volume</strong></td>
<td>2ml or more</td>
<td>2-6 ml</td>
<td>1.5ml</td>
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<tr>
<td><strong>Sperm count</strong></td>
<td>&gt;20 mil/ml</td>
<td>&gt;20 mil/ml</td>
<td>15 mil/ml</td>
</tr>
<tr>
<td><strong>Motility</strong></td>
<td>&gt;50% α</td>
<td>&gt;50% α + b</td>
<td>32%</td>
</tr>
<tr>
<td></td>
<td>&gt;25% α</td>
<td>&gt;25% α</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(within 60 minutes of ejaculation)</td>
<td>(within 60 minutes of ejaculation)</td>
<td></td>
</tr>
<tr>
<td><strong>Total motility</strong></td>
<td></td>
<td></td>
<td>40%</td>
</tr>
<tr>
<td><strong>Vitality</strong></td>
<td>≥60%</td>
<td>≥60%</td>
<td>58%</td>
</tr>
<tr>
<td><strong>Morphology</strong></td>
<td>15%</td>
<td>15%</td>
<td>4%</td>
</tr>
<tr>
<td><strong>Leucocytes</strong></td>
<td>&lt; 1 x 10⁶/ml</td>
<td>&lt; 1 x 10⁶/ml</td>
<td>&lt; 1 x 10⁶/ml</td>
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<tr>
<td><strong>MAR</strong></td>
<td>&lt; 50% motile spermatoza</td>
<td>&lt; 50% motile spermatoza</td>
<td>&lt; 50% motile spermatoza</td>
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Ejaculate volume

- spermia = ejaculate

• hypospermia (<2 ml)

• hyperspermia (>6 ml)
Sperm count

-zoospermia

– Normozoospermia **20 mil / mL**

– Azoospermia **No sperm in ejaculate**

– Oligozoospermia **< 20 mil / mL**

– Severe oligozoospermia **< 5 mil / mL**

– Polyzoospermia **Excessively high concentration >250mil/mL**
Sperm morphology

- **WHO**
- **Tygerberg strict criteria**

**Head**
- Smooth Oval
- Length 4-5 um
- Width 2.5-3.5um

**Mid piece**
- Width <1um

**Tail**
- 45um
Motility

asthenozoospermia

- partial – NB = lubricants
- total – Kartagener
- Supravital staining: alive/dead
Abnormal semen parameters

IF GP finds abnormal semen parameters - REFER!!!
Full evaluation for male infertility

• **Urologist/specialist**
  1. complete medical and reproductive history
  2. a physical examination
  3. at least two semen analyses

• **Based on these results - other procedures**
  – additional semen analyses
  – endocrine evaluation
  – post-ejaculatory urinalysis
  – Ultrasonography
  – specialized tests on semen and sperm,
  – genetic screening
Other procedures and tests for assessing male fertility

**Endocrine evaluation**

- not common causes of male infertility
- endocrine disorders are extremely uncommon in men with normal semen parameters

- endocrine evaluation should be performed
  - an abnormal semen analysis
  - impaired sexual function
  - clinical findings suggestive endocrinopathy
Other procedures and tests for assessing male fertility

**Endocrine evaluation**

- FSH, p-T
  - If p-T low, repeat total and free p-T, and prolactin (↑ levels)
- Many men with abnormal spermatogenesis have a normal serum FSH
- A marked **elevation of serum FSH** is clearly indicative of abnormal spermatogenesis.

Azoospermia + normal FSH = ductal obstruction
Azoospermia + elevated FSH = testicular failure
Other procedures and tests for assessing male fertility

*Post-ejaculatory urinalysis*

- Hypospermia or absent ejaculate suggests
  - retrograde ejaculation
  - lack of emission
  - ejaculatory duct obstruction
  - hypogonadism
  - CBAVD (congenital absence of the vas deferens)

**EXCLUDE**

improper or incomplete collection

very short abstinence period (less than 1 day)
Other procedures and tests for assessing male fertility

*Post-ejaculatory urinalysis*

Significant numbers of sperm in order to suggest the diagnosis of retrograde ejaculation
Other procedures and tests for assessing male fertility

**Ultrasonography**

- Transrectal ultra sonography (TRUS) in oligozoospermic patients
  - Hypospermia
  - Palpable vasa
  - Normal testicular size

- Scrotal ultrasonography may be useful to clarify ambiguous findings on examination
GENETIC SCREENING

Genetic abnormalities may affect sperm production or sperm transport.

• Three most common genetic factors related to male infertility:
  – cystic fibrosis gene mutations, CBAVD
  – chromosomal abnormalities - impaired testicular function
  – Y-chromosome microdeletions - isolated spermatogenic impairment
TREATMENT OF MALE INFERTILITY

“Hormonal imbalances” – NO!

1. Correctable/treatable
   - Surgery - vasovasostomy
   - Ejaculatory disorders
   - MAGI (male accessory gland infection)
   - Varicocele..... ??

2. ART – treat the woman for a male factor
   - IUI
   - IVF
   - ICSI
TREATMENT OF MALE INFERTILITY

Long term follow up essential

- Carcinoma in situ (CIS) testis
- Androgen deficiency ageing male – ADAM, PADAM
Thank you
Successful Sperm