Male infertility

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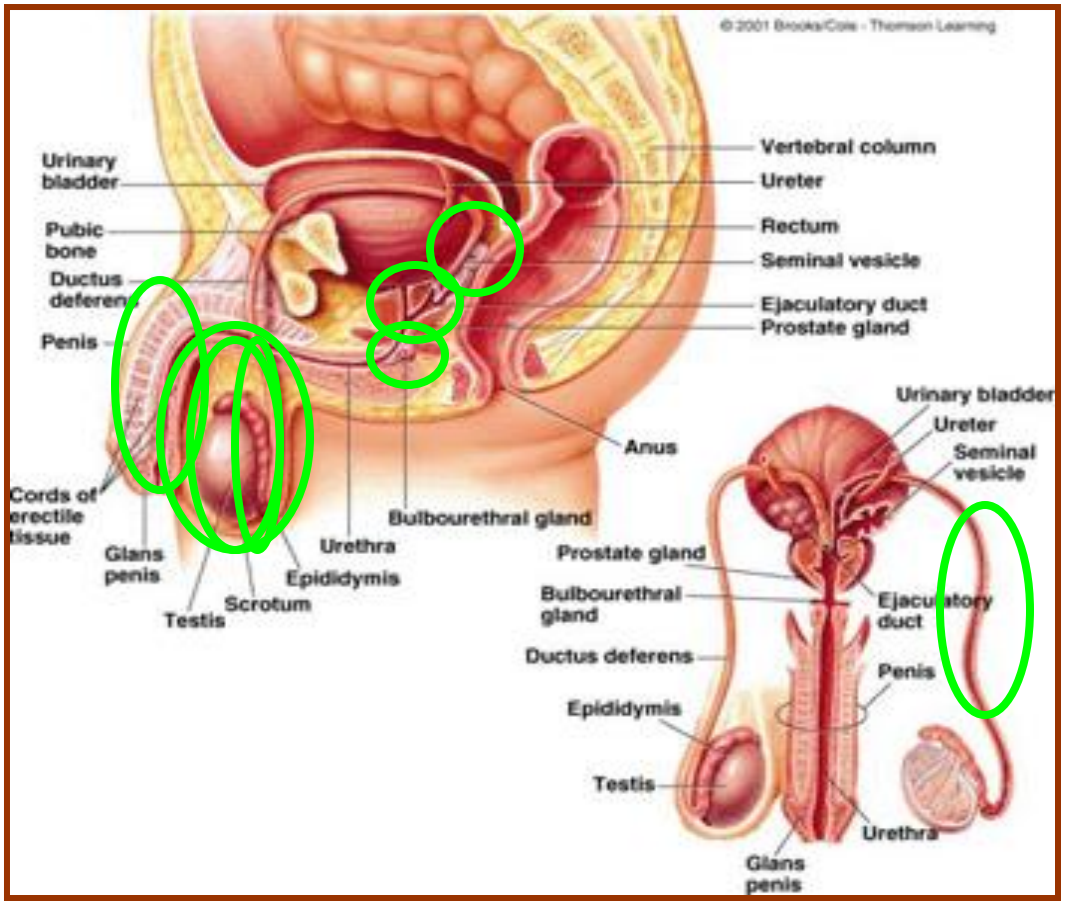
Outcomes

- 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

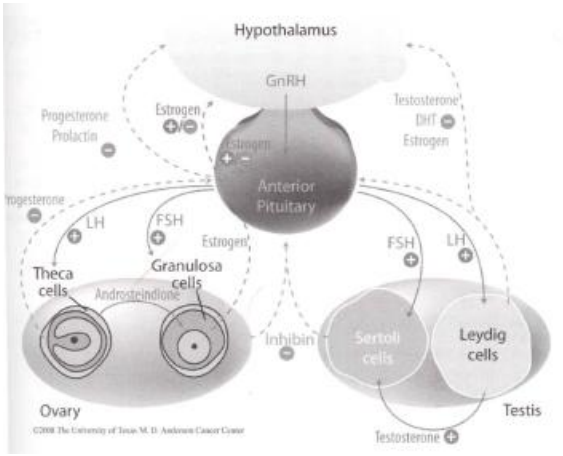
- The **hypothalamic-pituitary-gonadal axis** (**HPG axis**) refers to the effects of the hypothalamus, pituitary gland, and gonads as a single entity

- 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)



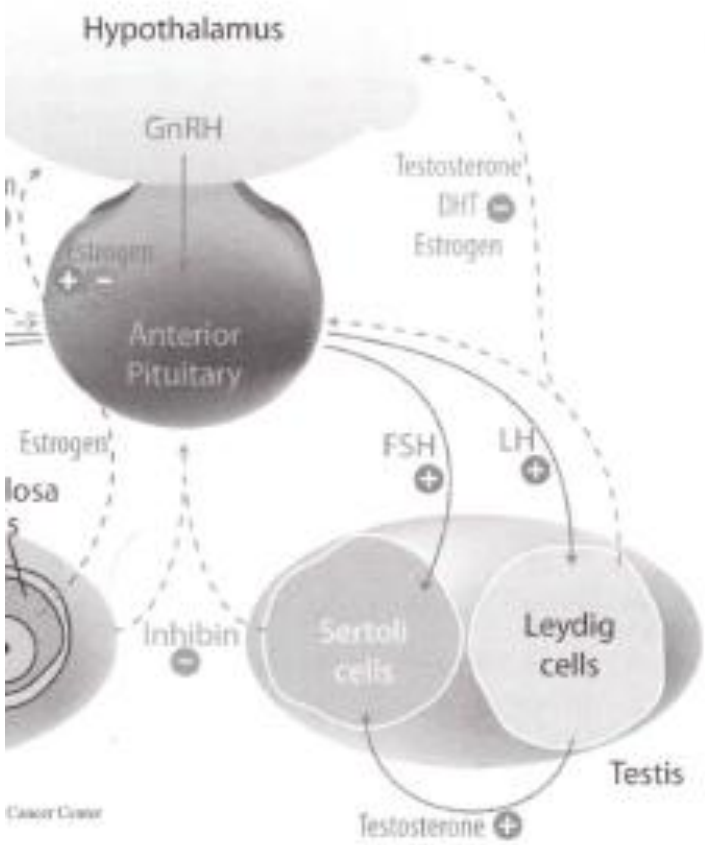
- The anterior portion of the pituitary gland produces
  - Luteinizing hormone (LH)
  - Follicle stimulating hormone (FSH)

- 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

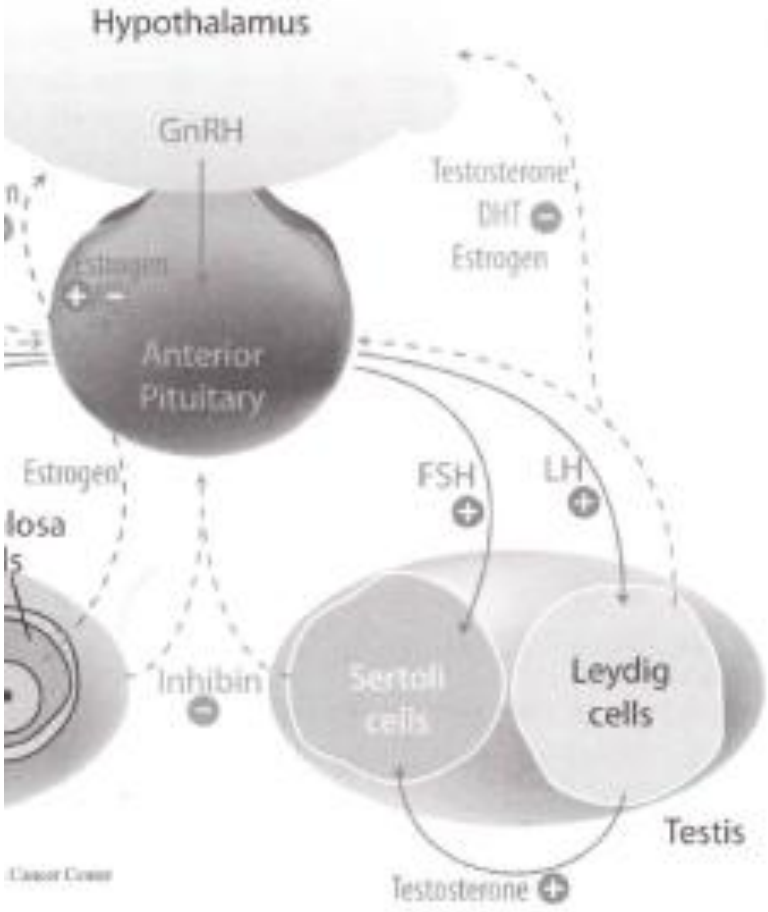


HPG-axis

In the pituitary

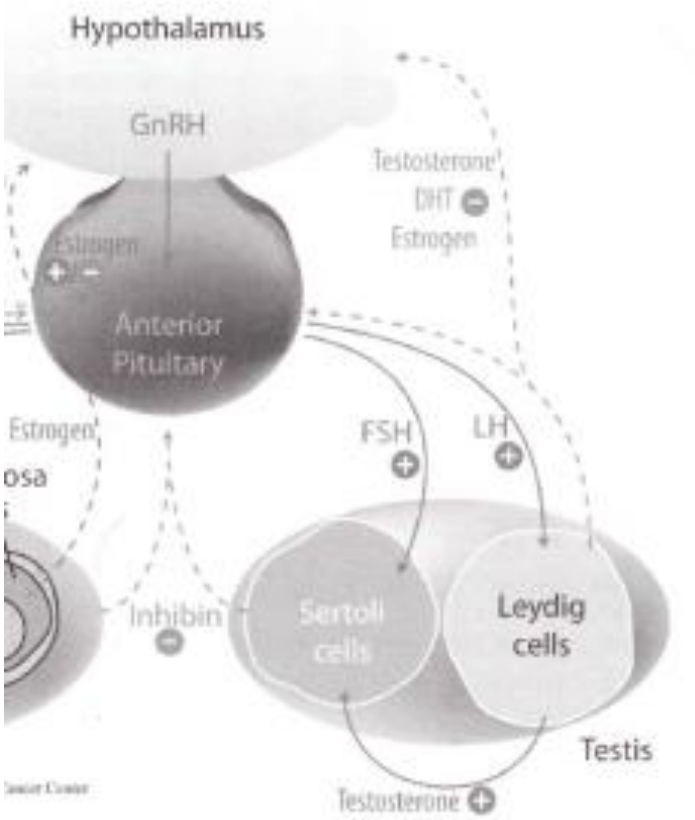
- GnRH receptors bind GnRH which induces the production and secretion of gonadotropins
  - Luteinizing hormone (LH)
  - Follicle stimulating hormone (FSH)

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



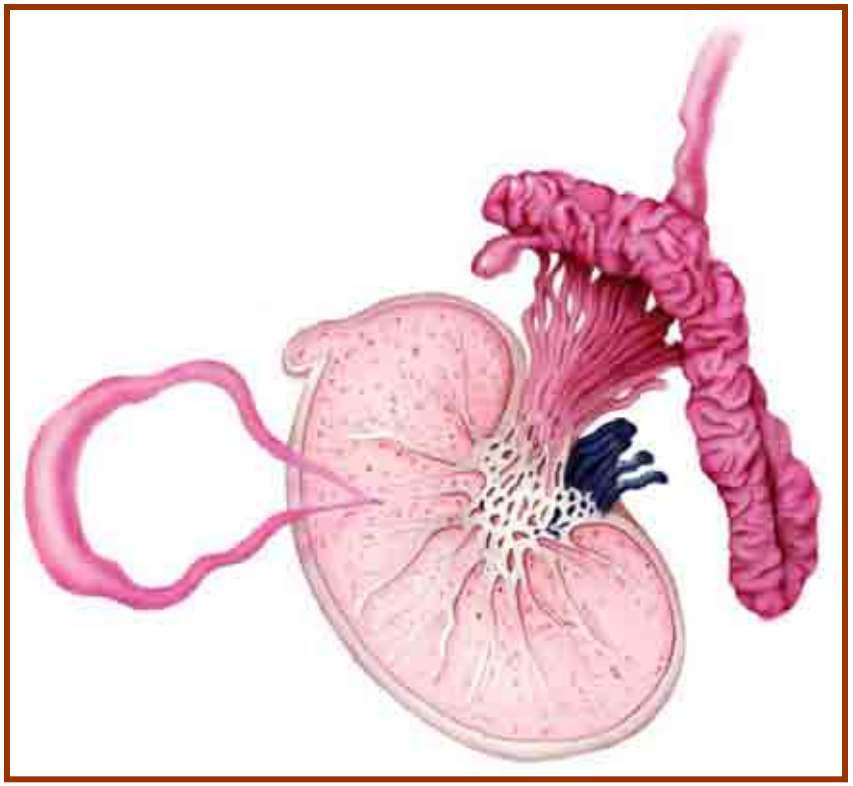
In the testis:

- 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



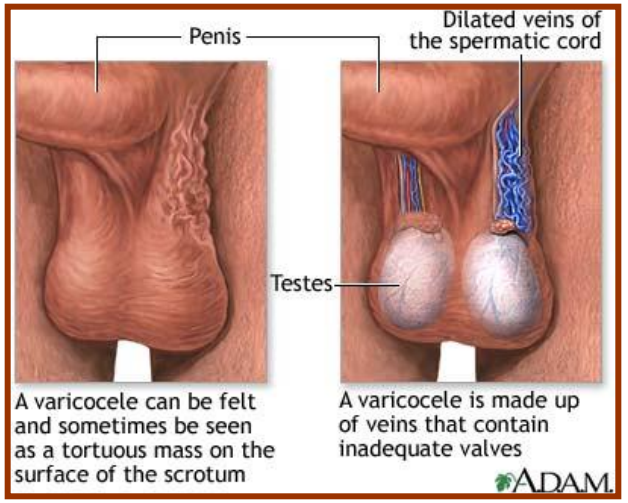
- Pre-testicular
- Testicular
- Post-testicular

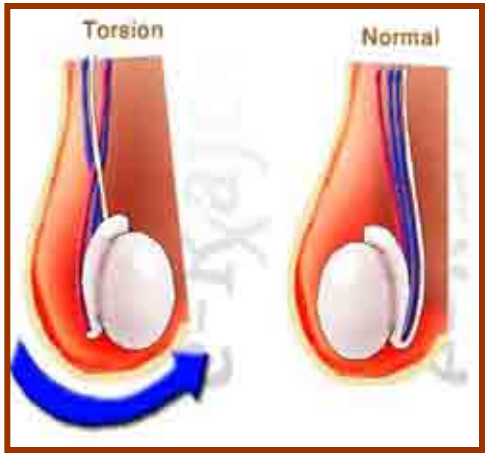
Causes –Pre-testicular

- 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

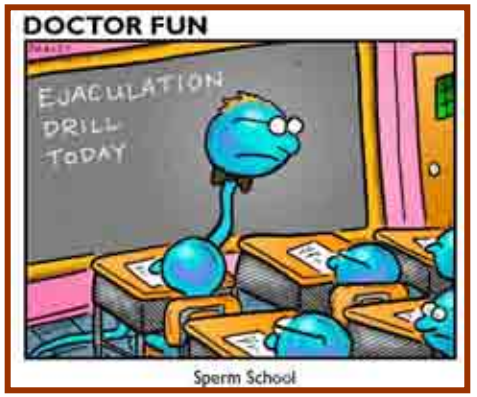
- Varicocele
- Undescended testes
- Previous testicular torsion/ trauma
- Mumps orchitis
- Radiotherapy
- Previous surgery (inguinal hernia repair)



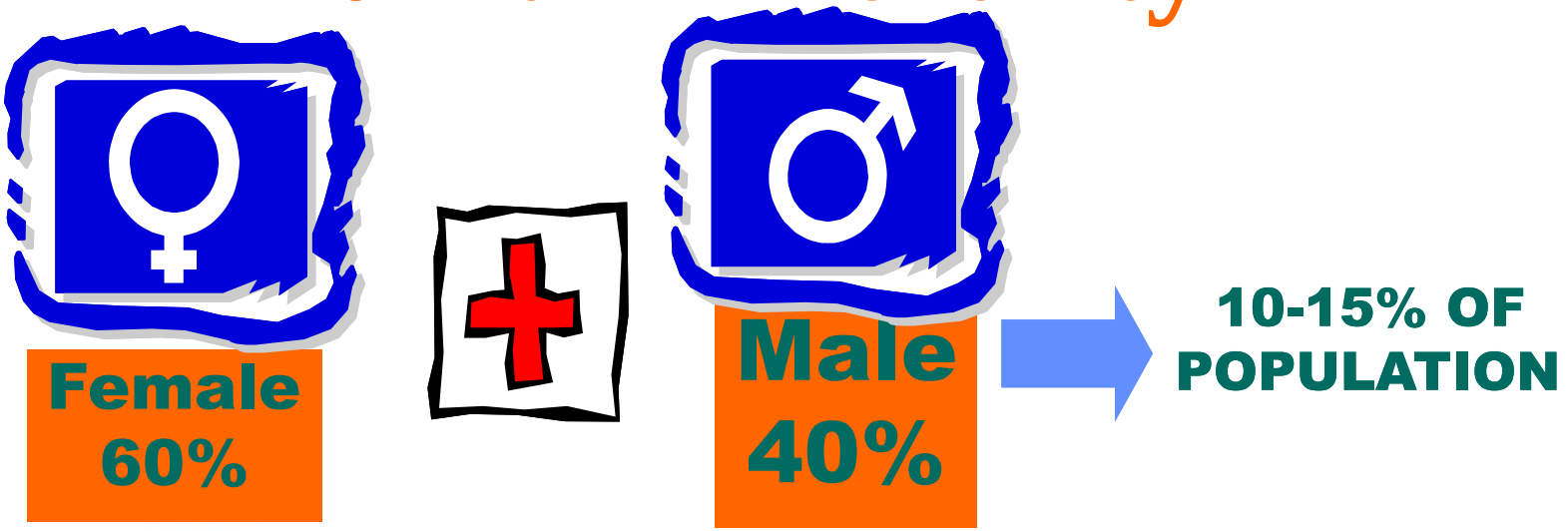


Causes – Post-testicular

- 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)

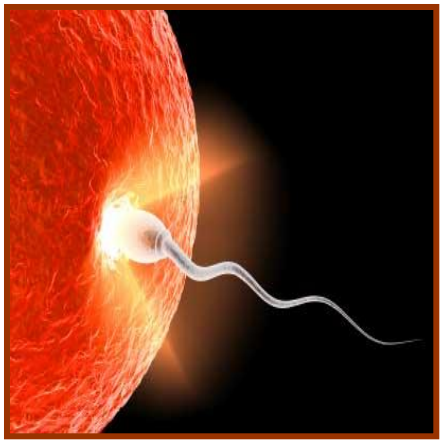


Human Infertility



Male infertility

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

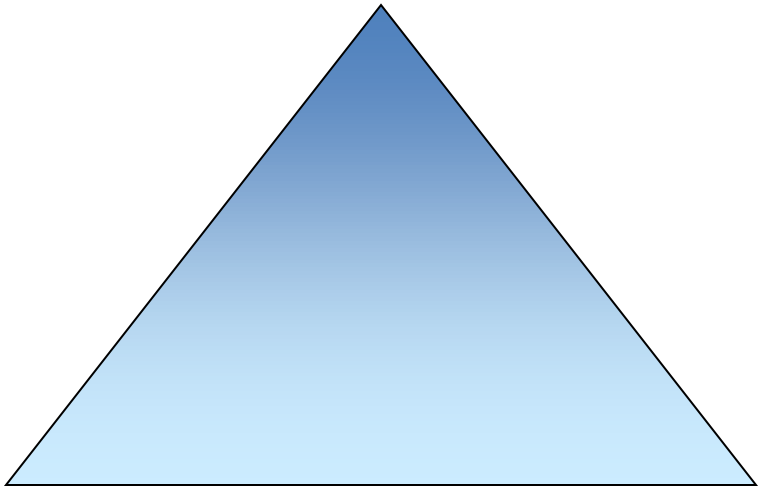


- male factor
  - solely responsible ~ 20%
  - contributory ~30-40%

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

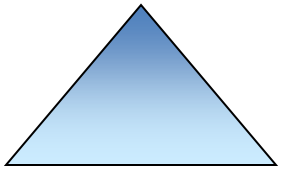
- genetic abnormalities that may affect the **health of offspring** if ART are to be employed.

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

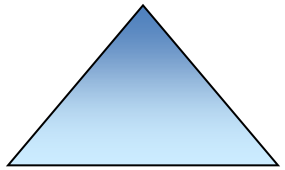
- coital frequency and timing
- duration and prior fertility
- childhood illnesses, developmental history
- systemic medical diseases (diabetes mellitus, upper respiratory tract)
- sexual history, STD, HIV
- gonadal toxin exposure, eg heat

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

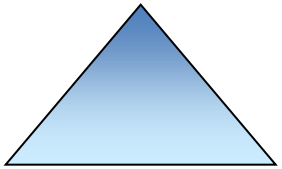
Required evaluation every patient



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



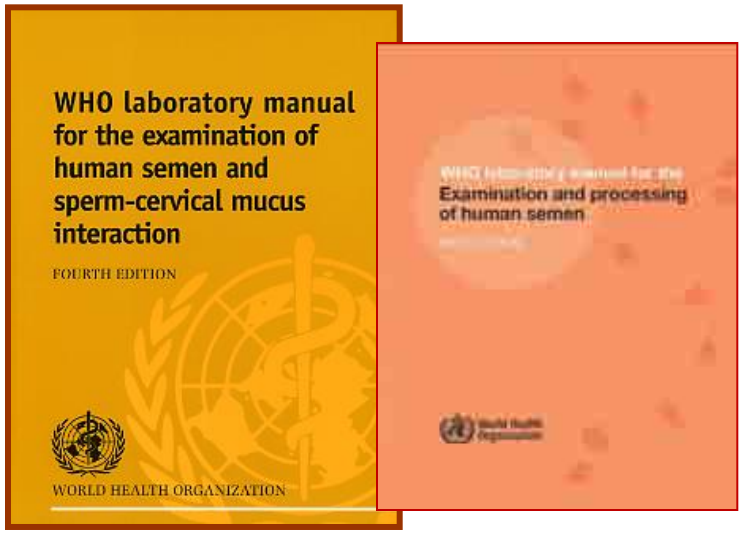
3. Semen analysis

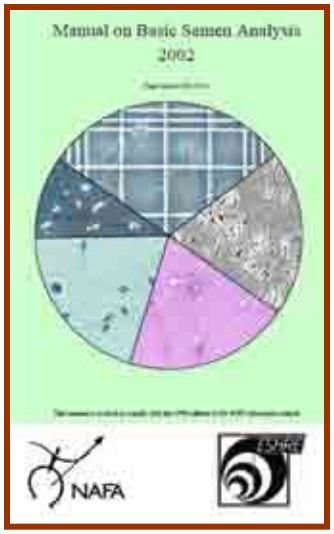
- cornerstone laboratory evaluation & helps to define the severity of the male factor
- methods of semen analysis: WHO
- accredited laboratory, trained technologist

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

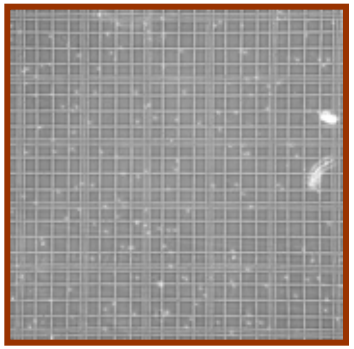
Semen analysis (WHO)

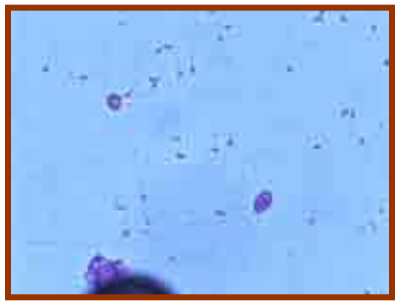




- **Standard instructions for semen collection:**
  - defined abstinence 3 days
  - masturbation, special collection condoms
  - collected at the laboratory
  - evaluated within one hour of collection
  - Quality Control Programme
  - expert technologist

Semen analysis (WHO)





- volume
- count
- motility
- morphology

EXCLUDE ARTEFACTS as possible causes of abnormal semen parameters

Semen = “hazardous”

- Contain harmful inf agents
  - HIV
  - Hepatitis
  - Herpes simplex

WHO (1999/2010): reference values semen analysis

	WHO 1999	ESHRE	WHO 2010
pH	7.2 or more	7.2 or more	> 7.2
Ejaculate volume	2ml or more	2-6 ml	1.5ml
Sperm count	>20 mil/ml	>20 mil/ml	15 mil/ml
Motility	>50% *a* *>25% a* *(within 60 minutes of ejaculation)*	>50% *a+b* *>25% a* *(within 60 minutes of ejaculation)*	32%
Total motility			40%
Vitality	≥60%	≥60%	58%
Morphology	15%	15%	4%
Leucocytes	< 1 x 10^6/ml	< 1 x 10^6/ml	< 1 x 10^6/ml
MAR	< 50% motile spermatozoa	< 50% motile spermatozoa	< 50% motile spermatozoa

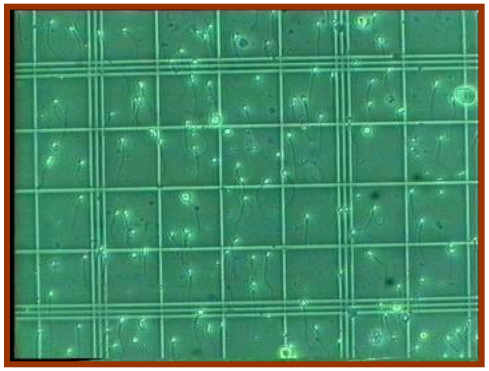
Ejaculate volume

-spermia = ejaculate

- hypospermia (<2 ml)
- hyperspermia (>6 ml)

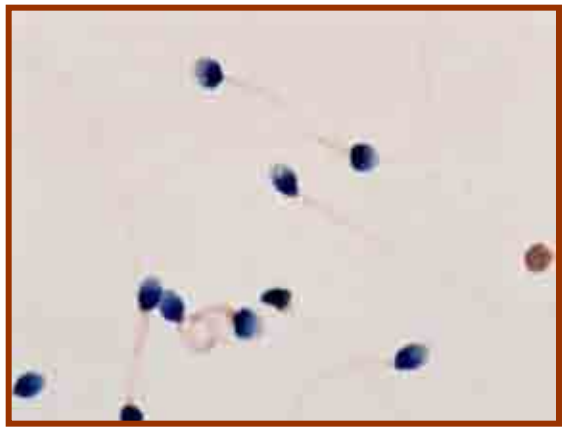
Sperm count

-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



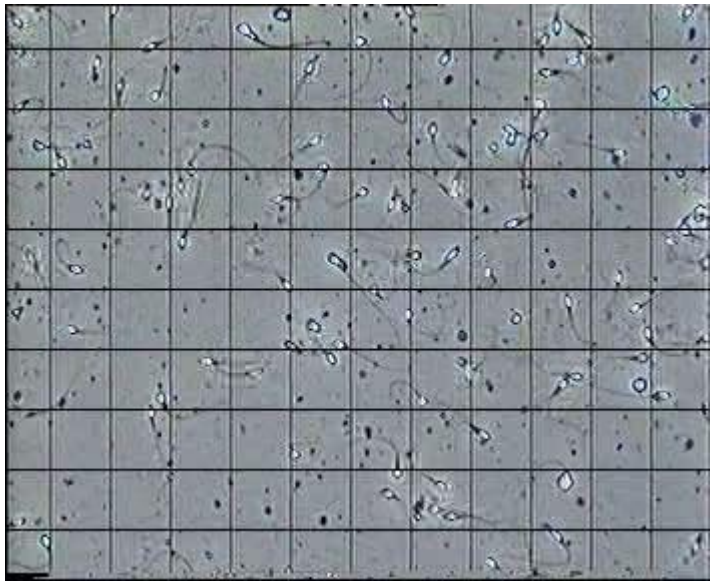
- WHO
- Tygerberg strict criteria

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)
   - Varicocoele..... ??

2. ART – treat the woman for a male factor
   - IUI
   - IVF
   - ICSI

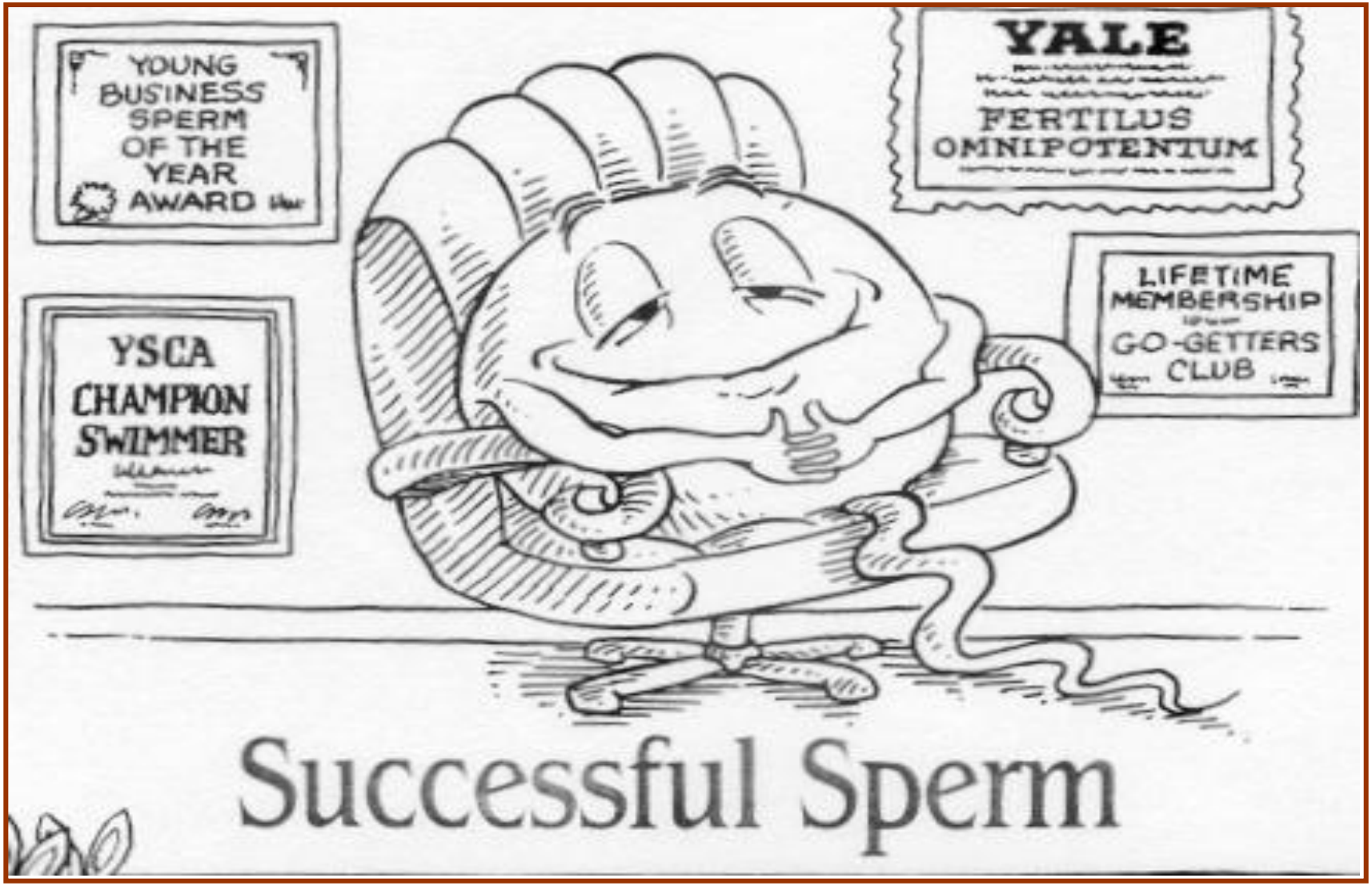
TREATMENT OF MALE INFERTILITY

Long term follow up essential

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

"See? You call my look 'a midlife crisis' but for these guys it's a major TV series."

Thank you


YOUNG BUSINESS SPERM OF THE YEAR AWARD
YALE
FERTILUS OMNIPOTENTIUM
LIFETIME MEMBERSHIP
GO-GETTERS CLUB
YSCA CHAMPION SWIMMER
Successful Sperm