

Workshop E:

Navigating male fertility assessments and managing challenging cases

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OBJECTIVES

As a result of attending this session, participants will be able to:

- Outline the common pitfalls in the assessment of infertile couples
- Identify clues that required prompt referral to specialists
- Differentiate various forms of assisted reproductive technologies in the management of male infertility



ARTs – Assisted Reproductive Technologies

IUI: Intra-Uterine Insemination

IVF: In Vitro Fertilization

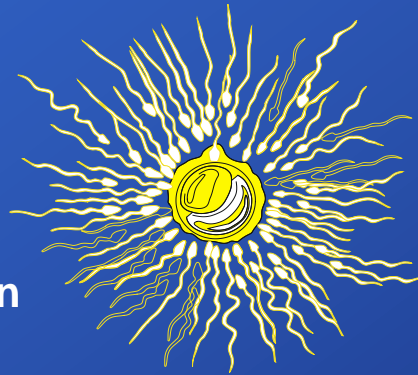
ICSI: Intra-Cytoplasmic Sperm Injection



ARTs – Assisted Reproductive Technologies

Natural

> 20 million



IUI

> 5-10 million



IVF

>1 million



ICSI

1 sperm !



MALE FERTILITY EVALUATIONS

- History & Physical Exam
- Semen analyses
- Blood tests

1. Find out any reversible causes of infertility
2. Find out any serious underlying diseases



HISTORY – WHAT QUESTIONS TO ASK

- Duration of infertility and previous history of fecundity
- Previous fertility treatments
- Developmental history and childhood illnesses
- Coital frequency/timing? history of STI's? Erectile dysfunction?

(Chan, Rosenwaks and Goldstein, In: "Reproductive Medicine Secrets", 2004.)

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ED - ERECTILE DYSFUNCTION

- Up to 35% of men undergoing fertility treatment have ED
- Less frequent intercourse → decreased likelihood of pregnancy
- Hypogonadism
- Complex psychosocial stress



TOOLS FOR EVALUATING ED

SHIM – SEXUAL HEALTH INVENTORY FOR MEN QUESTIONNAIRE

- 1. How often were you able to get an erection during sexual activity?*
- 2. When you had erections with sexual stimulation, how often were your erection hard enough for penetration?*
- 3. When you attempted intercourse, how often were you able to actually penetrate your partner?*
- 4. During sexual intercourse, how often were you able to maintain your erection after you had penetrated your partner?*
- 5. During sexual intercourse, how difficult was it to maintain your erection to completion of intercourse?*
- 6. If you were to spend the rest of your life with your erectile condition the way it is now, how would you feel about that?*



TOOLS FOR EVALUATING ED

SHIM – SEXUAL HEALTH INVENTORY FOR MEN QUESTIONNAIRE

<u>SHIM SCORE</u>	<u>ED status</u>
26-30	No ED
22-25	Mild ED
17-21	Mild to moderate ED
11-16	Moderate ED
6-10	Severe ED



HISTORY – WHAT QUESTIONS TO ASK

- Duration of infertility and previous history of fecundity
- Previous fertility treatments
- Developmental history and childhood illnesses
- Coital frequency/timing? history of STI's? Erectile dysfunction?
- Systemic medical illnesses and surgical history
- Family history of fertility and systemic illnesses
- Life style and psychosocial stress factors
- Exposure to gonadotoxins and heat.

(Chan, Rosenwaks and Goldstein, In: "Reproductive Medicine Secrets", 2004.)

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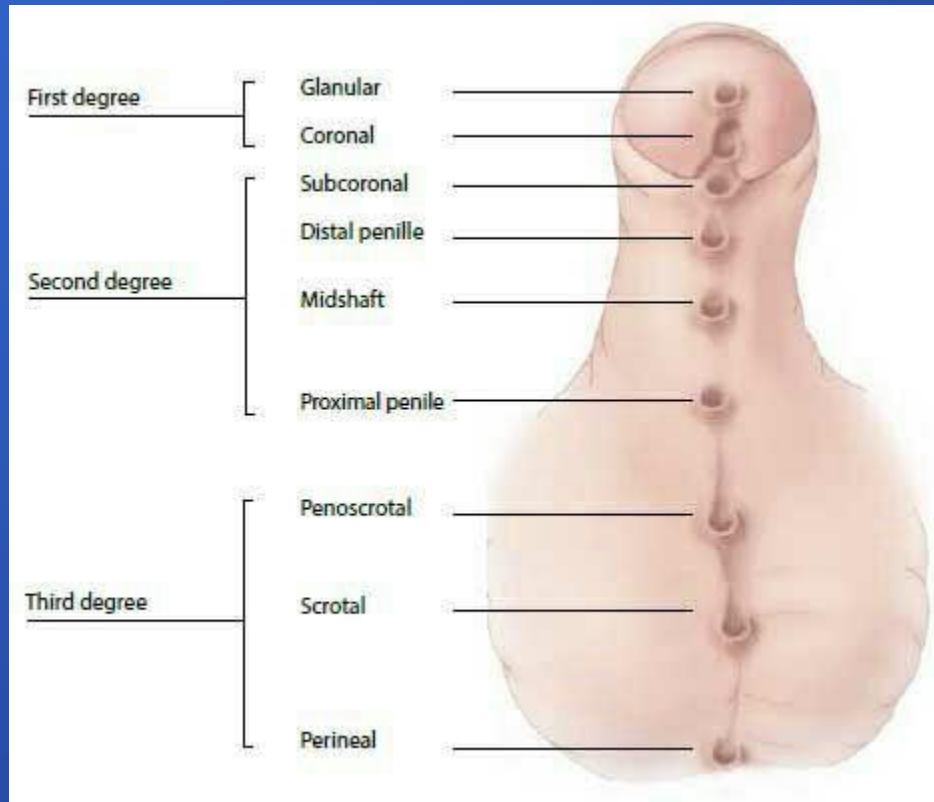


PHYSICAL EXAMINATION

- General physique, secondary sexual characteristics
- Stigmata of genetic anomalies
- Penis anatomy, urethral opening location
- Testes size and texture

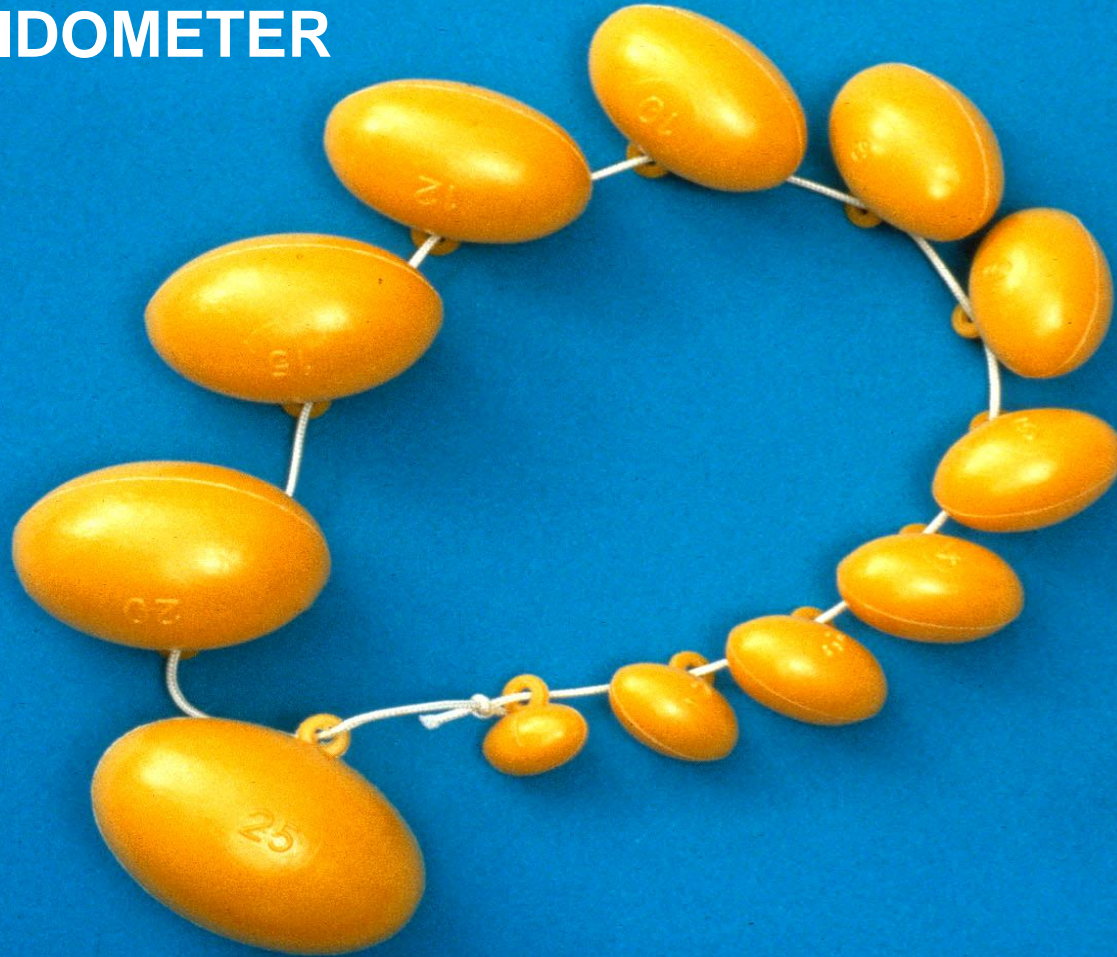


HYPOSPADIUS



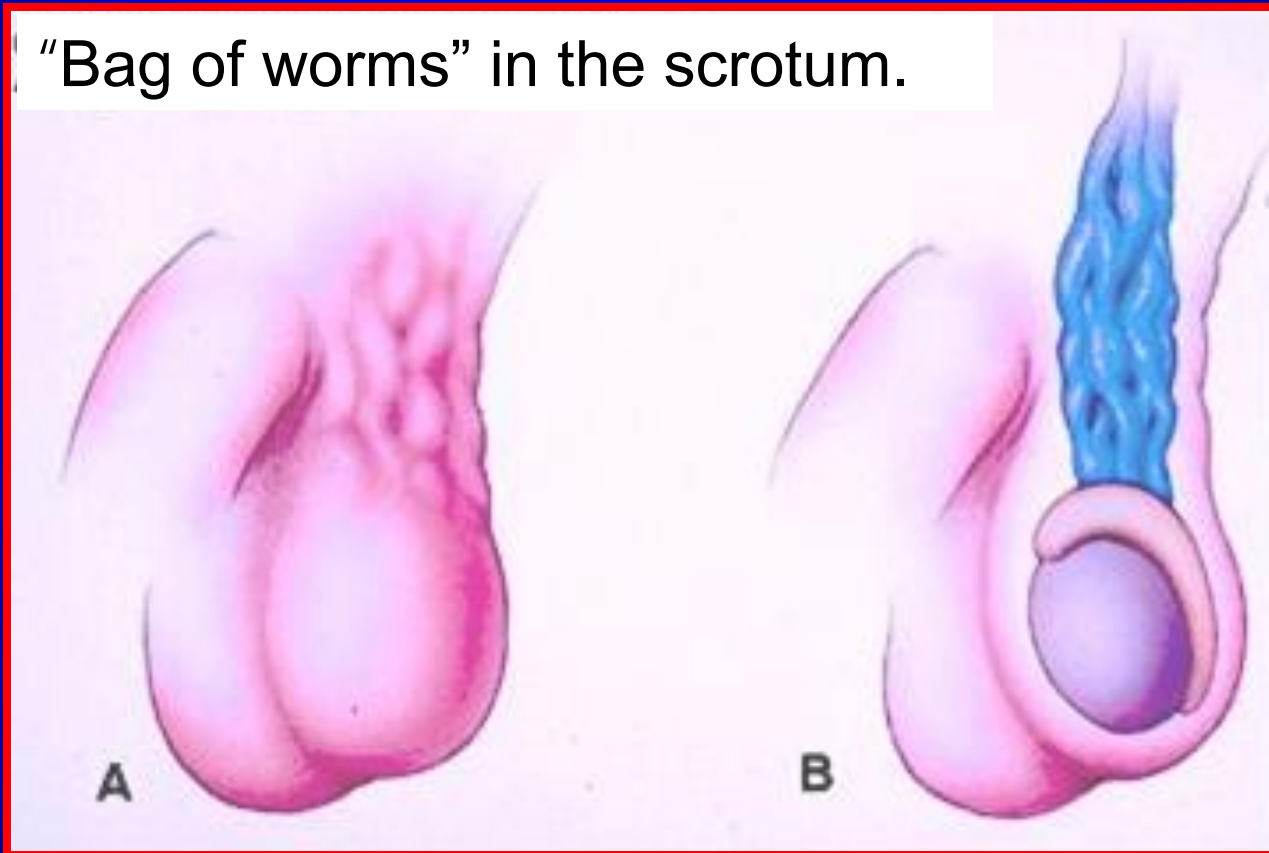
PHYSICAL EXAMINATION

ORCHIDOMETER



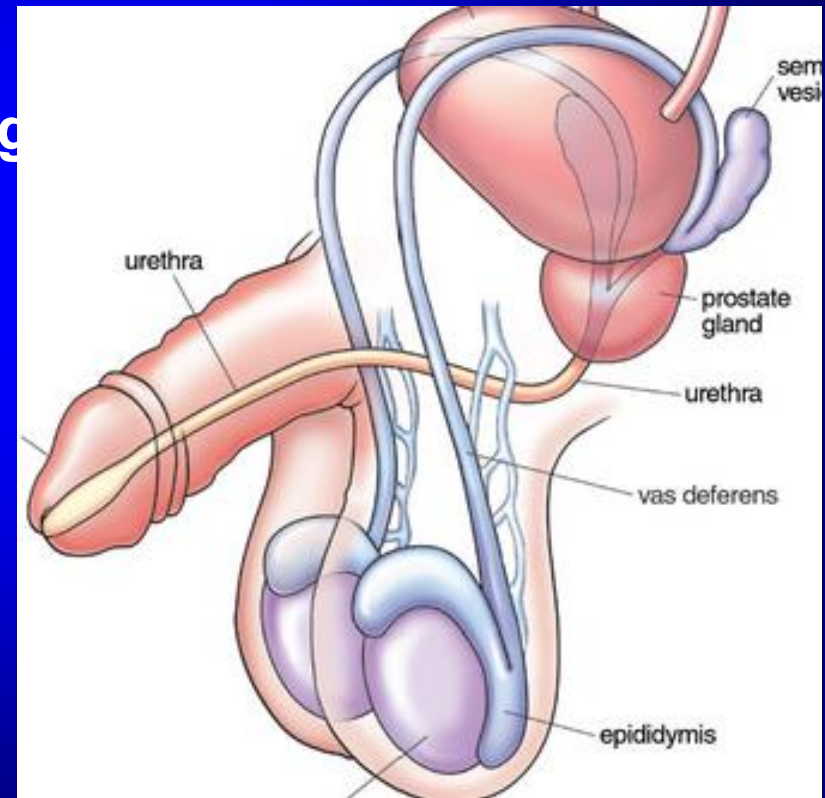
Varicoceles

"Bag of worms" in the scrotum.



PHYSICAL EXAMINATION

- General physique, secondary sexual characteristics
- Stigmata of genetic anomalies
- Penis anatomy, urethral opening
- Testes size and texture
- Varicoceles
- Vasa deferentia



(Chan, Rosenwaks and Goldstein, In: "Reproductive Medicine Secrets", 2004.)

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PHYSICAL EXAMINATION

- General physique, secondary sexual characteristics
- Stigmata of genetic anomalies
- Penis anatomy, urethral opening location
- Testes size and texture
- Varicoceles
- Vasa deferentia
- Testicular mass



(Chan, Rosenwaks and Goldstein, In: "Reproductive Medicine Secrets", 2004.)

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SEMEN ANALYSES

- Most commonly used investigation for male fertility evaluation
- Main parameters: sperm concentration, motility, morphology.



Semen analysis

1. Most commonly used evaluation of male fertility
2. Highly susceptible to inter-lab variation, operator variation and intra-individual variation.
3. To minimize variation, should do at least 2 analyses with > 2 months apart
4. Observe abstinence period of ~3 days. No febrile illnesses > 2 months.
5. Masturbation into a wide mouth container. No lubricants
6. Issues with masturbation



HOW TO EVALUATE MALE FERTILITY?

- **History & Physical Exam**

- **Semen analyses**

- **Blood tests**

Gonadotropins: FSH, LH

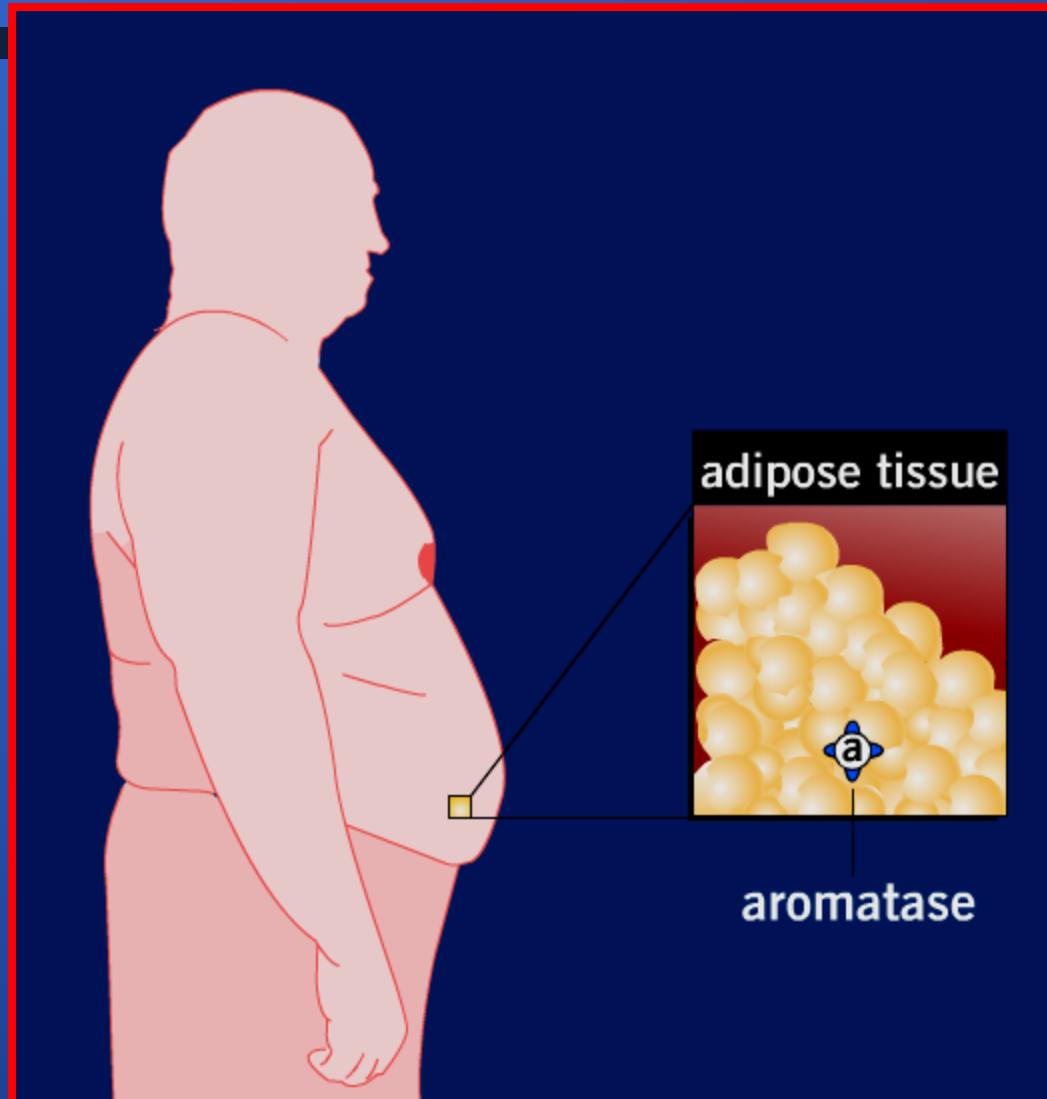
Morning total testosterone

Estradiol

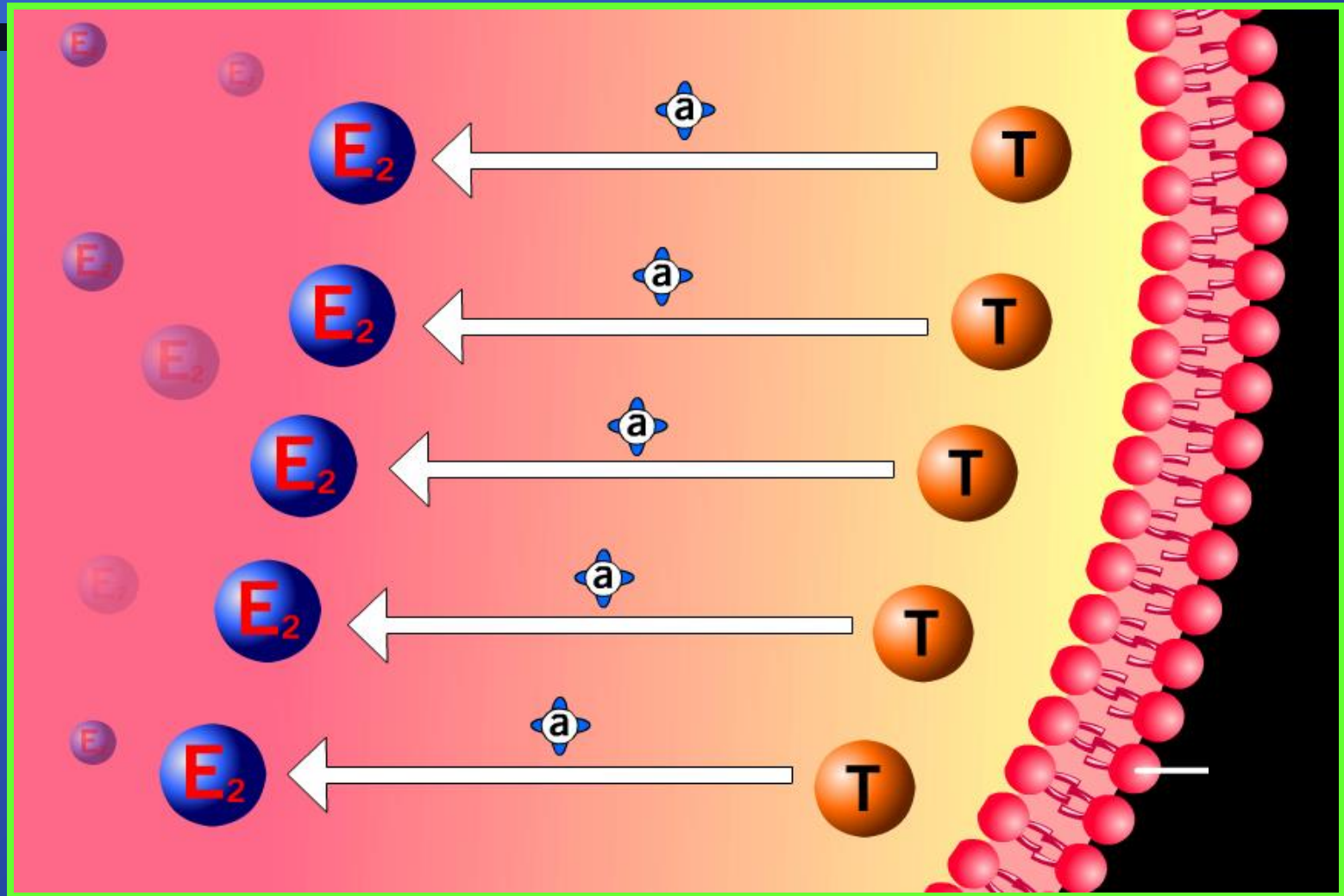
(Bio-available testosterone, TSH, prolactin)



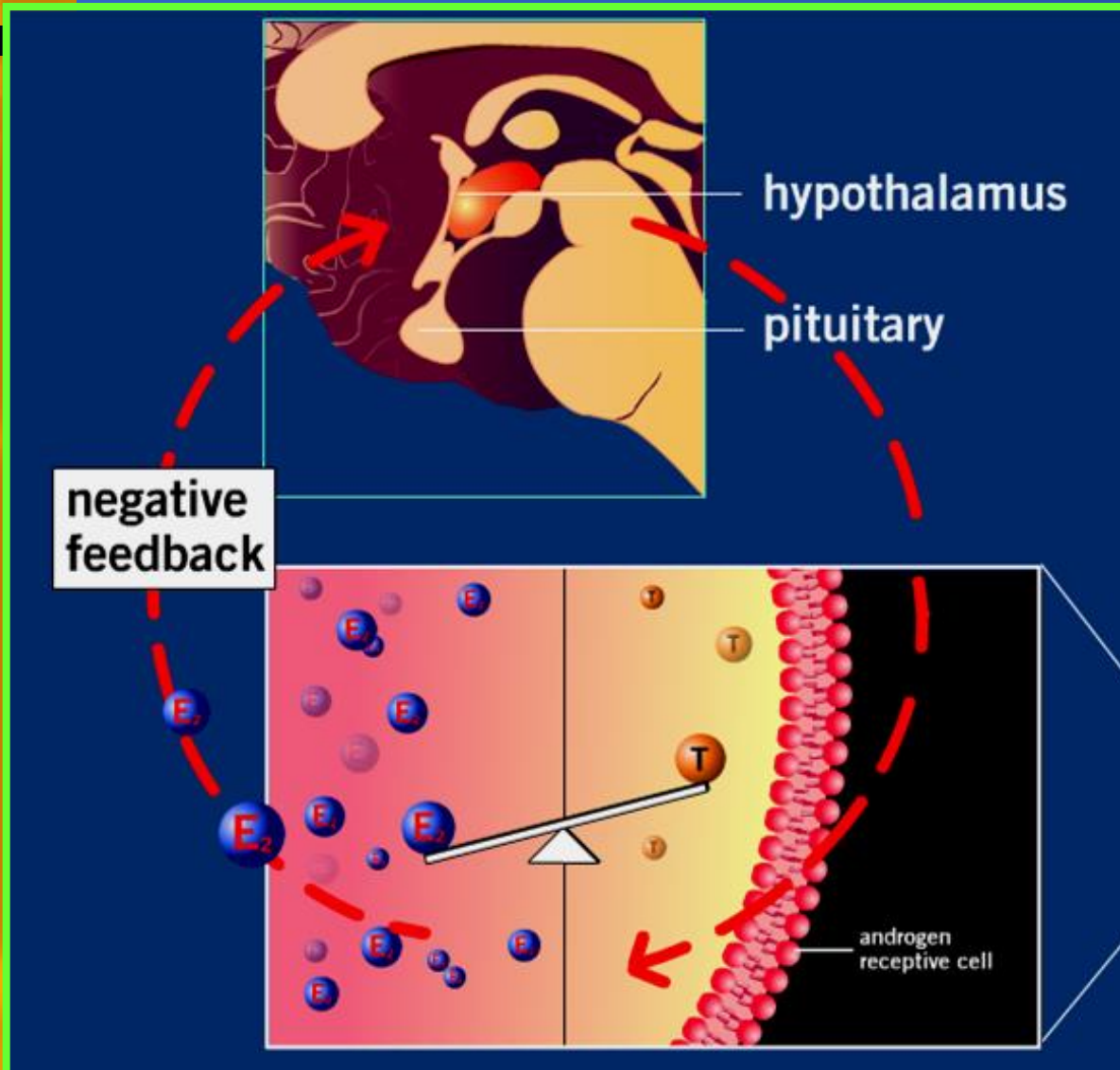
WHY IS OBESITY BAD FOR SPERM?



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WHY IS OBESITY BAD FOR SPERM?



Testosterone ↓

E₂ ↑

FSH ↓

Spermatogenesis ↓



CASE 1

- A 35 yo previously healthy man and his 35 yo healthy partner tried >1 yr with no success. He complained of loss in libido for the passed 3 months.

Which of the following options would you recommend for this man?

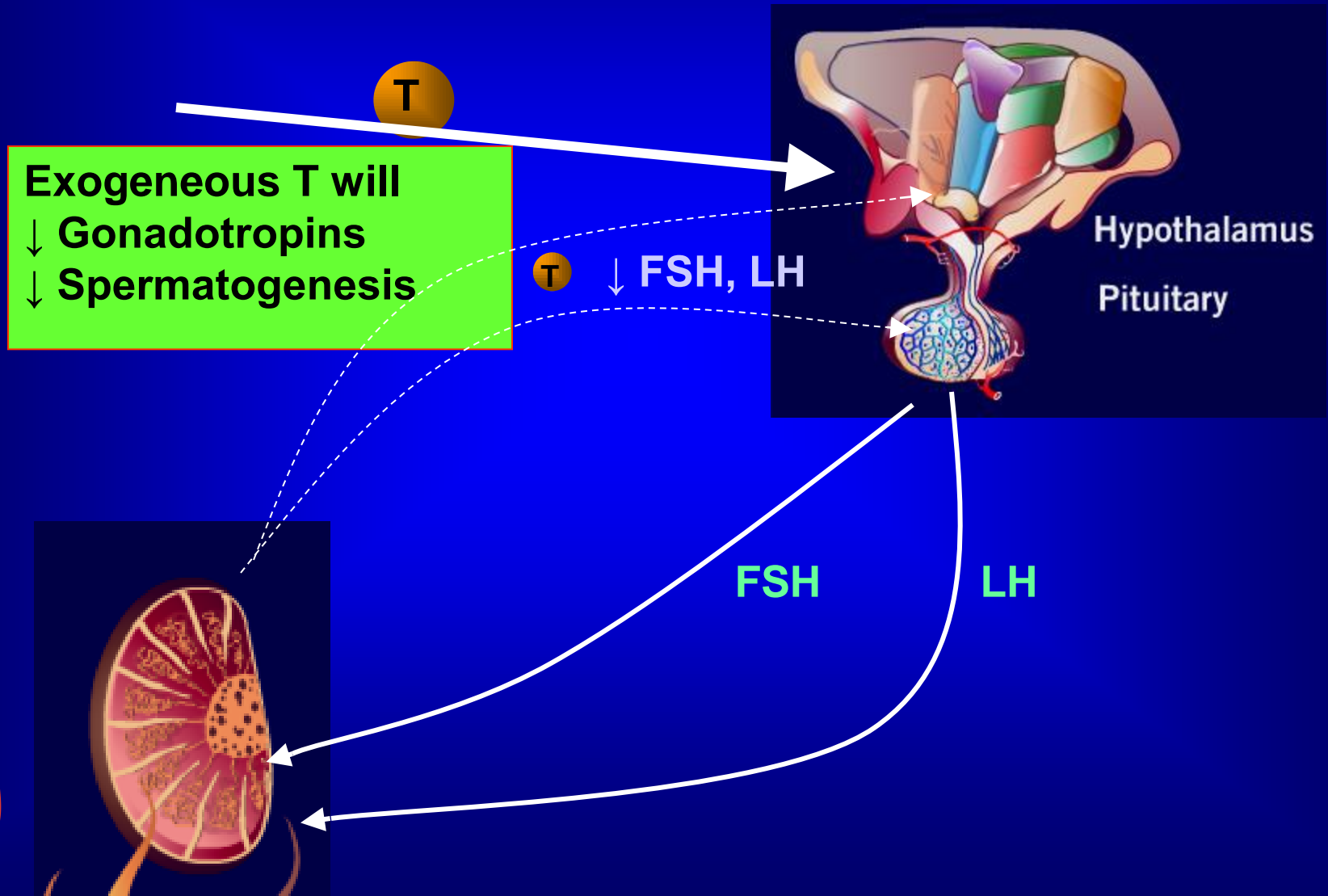
1. PDE5-inhibitors
2. Antibiotics
3. Anti-oxidants/vitamins
4. Testosterone supplements
5. Antidepressants

TESTS	RESULTS	REF
Sperm counts:	10 million/ml	(>16)
Progressive motility:	27%	(>30)
Morphology:	5%	(4)
FSH	6 IU/ml	(2-12)
LH	8 IU/ml	(2-12)
Total testosterone	6.5 nmol/ml	(10-24)

Normal Prolactin, TSH and Estradiol



WHY NOT JUST GIVE THEM TESTOSTERONE?



TESTOSTERONE – PROTOTYPE FOR MALE CONTRACEPTIVES

- High dose T-enantate (100 or 300 mg/wk)
 - 50-70% men achieve azoospermia (*Matsumoto 1990; Garrett et al., 2005*)
- T combine with progestin or medroxyprogesterone
 - faster suppression of spermatogenesis (*Ly et al., 2005; McLachlan et al., 2008*)



CASE 2

- A 44 yo healthy man failed to achieve pregnancy for two years with his 29 year old ex-wife. On physical exam you found left sided varicoceles. He denied any testicular pain or sexual problems. He requested to have a sperm tests because he is trying for 1 yr to have children with his new 42 yo girlfriend.

TESTS	RESULTS	REF
Sperm counts:	18 million/ml	(>16)
Progressive motility:	28%	(>30)
Morphology:	3%	(4)

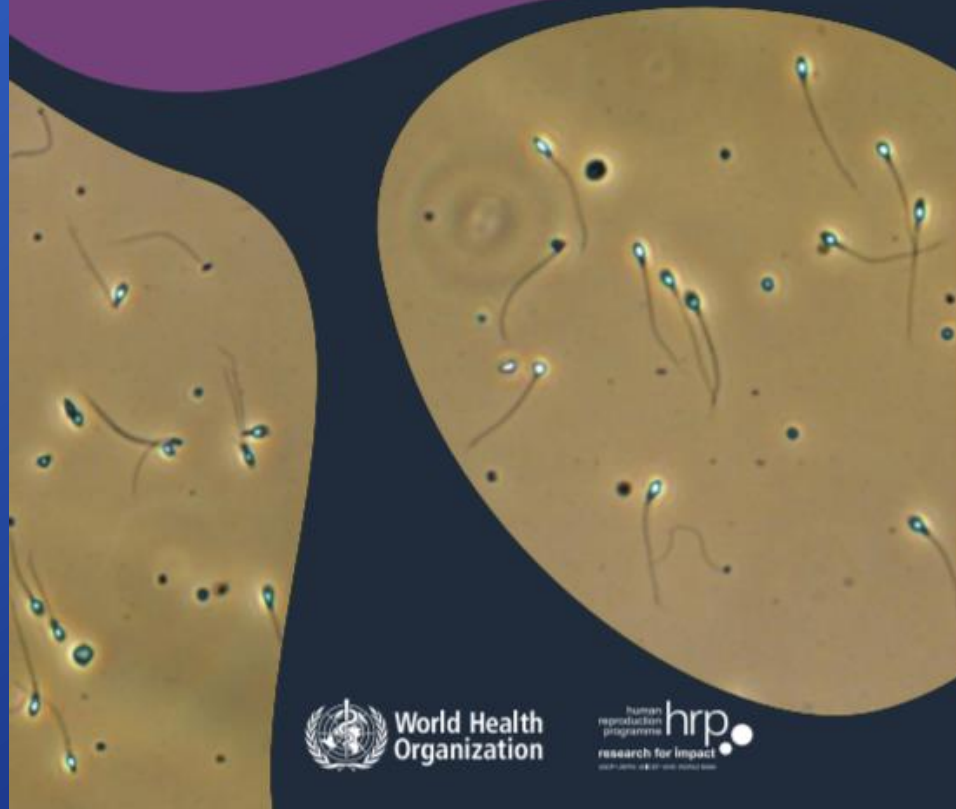
Which are you thoughts on the following statements?

1. His ex-wife is likely the cause of previous infertility
2. His varicoceles has no impact on his reproductive health
3. He is fertile and no further investigations on him is required
4. His current wife should start fertility evaluation



WHO laboratory manual for the
**examination and processing of
human semen**

Sixth Edition



WHO REFERENCE VALUES

- **What are “reference” values??**

The averages of the population parameters? NO!

The minimum to be considered fertile? NO!

Above them means you are fertile? NO!

Below them means you are infertile? NO!



SEMEN ANALYSIS - INTERPRETATION

	N	Centiles									
		2.5th	5th	(95% CI)	10th	25th	50th	75th	90th	95th	97.5th
Semen volume (ml)	3586	1.0	1.4	(1.3-1.5)	1.8	2.3	3.0	4.2	5.5	6.2	6.9
Sperm concentration (10 ⁶ per ml)	3587	11	16	(15-18)	22	36	66	110	166	208	254
Total sperm number (10 ⁶ per ejaculate)	3584	29	39	(35-40)	58	108	210	363	561	701	865
Total motility (PR + NP, %)	3488	35	42	(40-43)	47	55	64	73	83	90	92
Progressive motility (PR, %)	3389	24	30	(29-31)	36	45	55	63	71	77	81
Non-progressive motility (NP, %)	3387	1	1	(1-1)	2	4	8	15	26	32	38
Immotile spermatozoa (IM, %)	2800	15	20	(19-20)	23	30	37	45	53	58	65
Vitality (%)	1337	45	54	(50-56)	60	69	78	88	95	97	98
Normal forms (%)	3335	3	4	(3.9-4.0)	5	8	14	23	32	39	45



CASE 3

- Telemedicine consultation:

A 37 yo healthy man have a daughter with his 39 yo wife 3 yrs ago using IUI in Toronto. They have retried for 8 months naturally with no success and would like to be referred for IUI in Montreal. He repeated his sperm tests recently:

TESTS	RESULTS	REF
Sperm counts:	6 million/ml	(>16)
Progressive motility:	12%	(>30)
Morphology:	1%	(4)

Which are you thoughts on the following statements?

1. Refer them.
2. Tell them to try 4 more months before referral
3. Arrange for blood tests.
4. He should come in for a physical exam prior to referral.



Reasons for Evaluation of Male Fertility

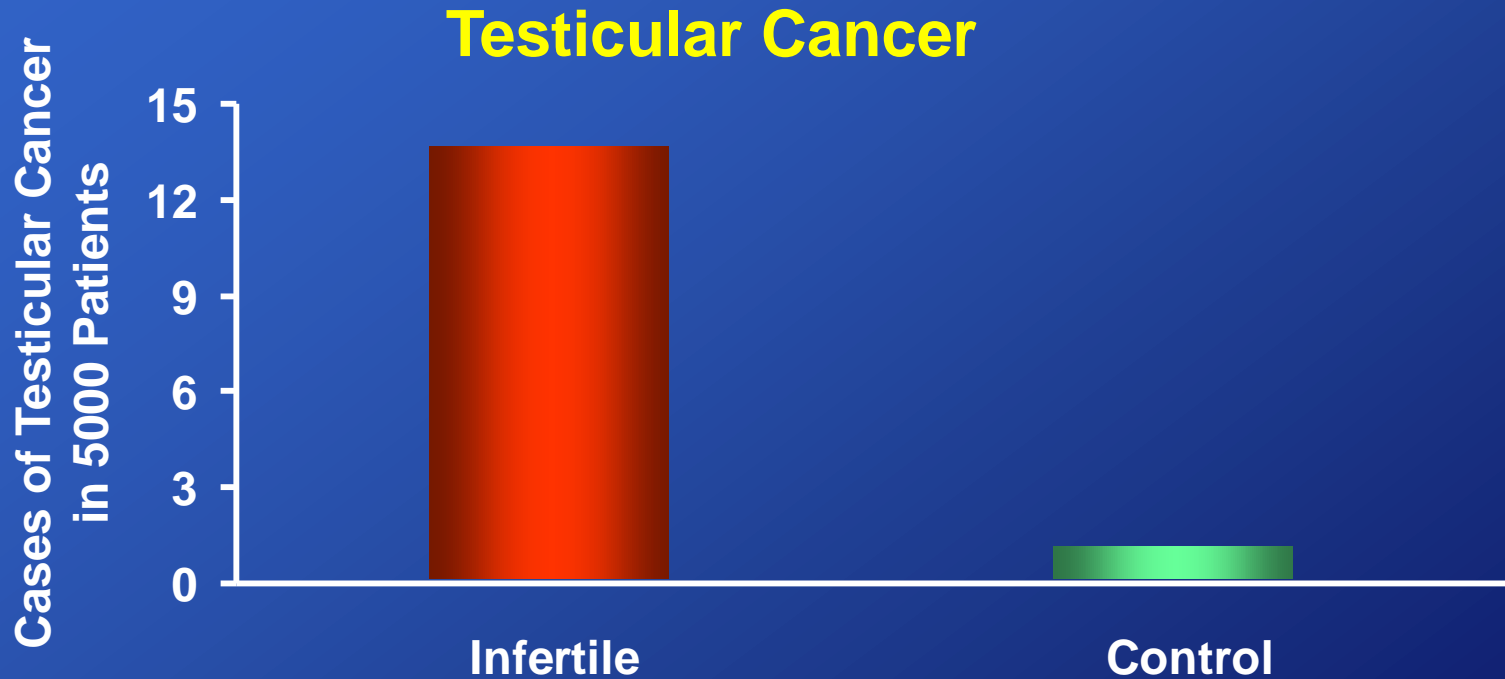
- **Male infertility**

→ **severe underlying illnesses**

- **Testicular cancer**
- **Osteoporosis**
- **Hormonal disorders**
- **Genetic disorders**



Series Conditions in Male Infertility



Infertile men are over 20 times more likely to have testicular cancer

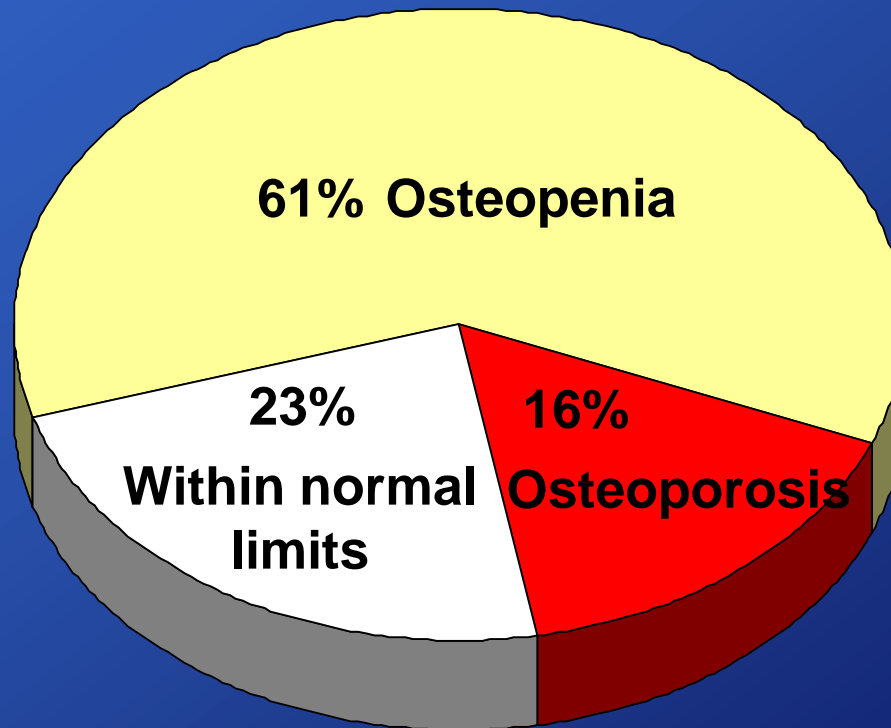
Raman et al., J Urol. 2005 Nov;174(5):1819-22



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Series Conditions in Male Infertility

Osteoporosis/Osteopenia



Mean age
35 years

Chan PTK, Schlegel PN. Presented at the Annual Meeting of the American Urological Association; June 2-7, 2001; Anaheim, CA. Abstract 1435.

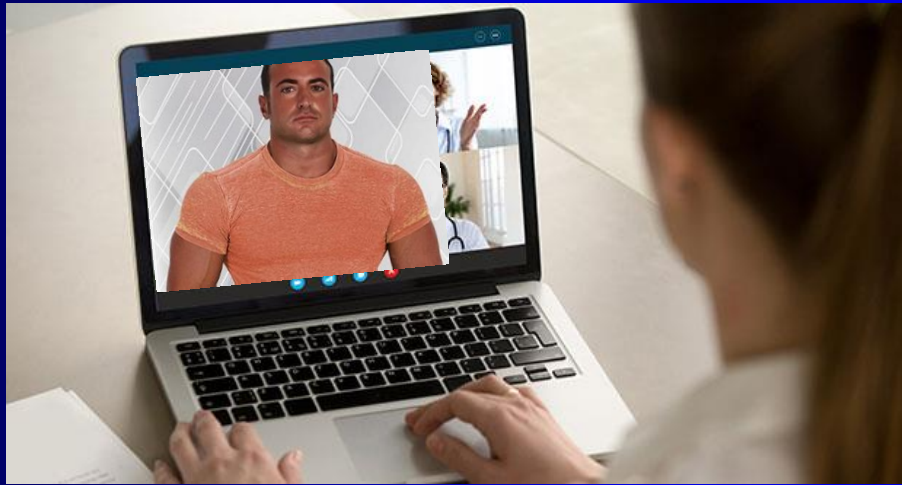
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CASE 4

- Telemedicine consultation:

A 30 yo healthy man had a daughter 3 yrs ago with his current 29 year old girlfriend. They have now retried for 8 months with no success. He takes no medications or supplements and has no previous surgery.



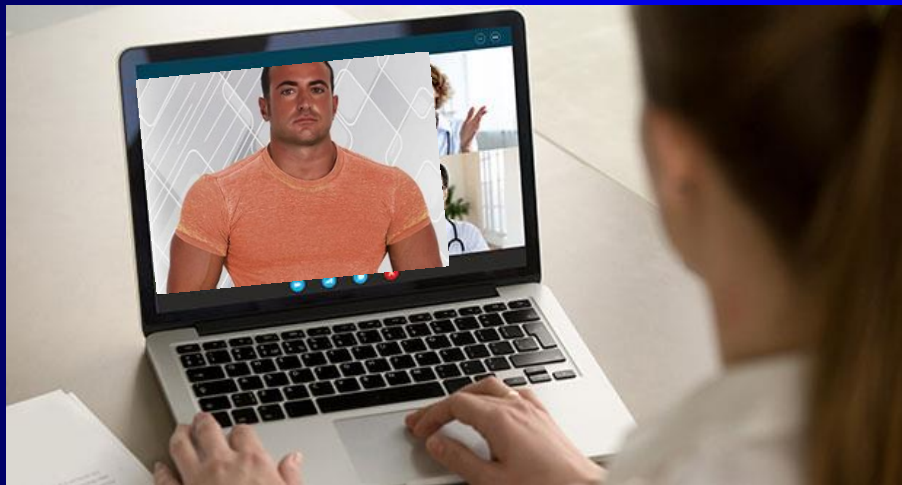
TESTS	RESULTS	REF
Sperm counts:	<1 million/ml	(>16)
Progressive motility:	0%	(>30)
Morphology:	---	(4)
FSH	0.8 IU/ml	(2-12)
LH	0.6 IU/ml	(2-12)
Total testosterone	22 nmol/ml	(10-24)

Normal Prolactin, TSH and Estradiol



CASE 4

- What if his total testosterone is also low at 4 nmol/ml?



TESTS	RESULTS	REF
Sperm counts:	1 million/ml	(>16)
Progressive motility:	6%	(>30)
Morphology:	4%	(4)
FSH	0.8 IU/ml	(2-12)
LH	0.6 IU/ml	(2-12)
Total testosterone	4 nmol/ml	(10-24)

Normal Prolactin, TSH and Estradiol



WHEN TO REFER (PROMPTLY)?

- Female age > 37 yrs
- Suspicious testicular mass
- Azoospermia/severe oligospermia
- Recurrent pregnancy loss
- Newly diagnosed conditions that require cytotoxic therapy or surgery that would impair fertility

