

Male fertility assessment: What can I do in the office?

Peter Chan, MD, CM, M.Sc., FRCS(C), FACS

Past President, Society of Reproductive Surgeons,
Director of Male Reproductive Medicine,
Professor, Department of Urology, McGill University Health Center
Montreal, Canada



OBJECTIVES

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

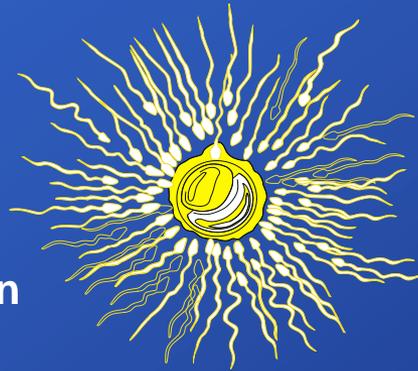
- Outline the basic evaluation of male reproductive health in the primary care setting
- Describe the common additional investigations to assess male infertility
- Formulate the initial management strategies of some challenging male infertility cases



ARTs – Assisted Reproductive Technologies

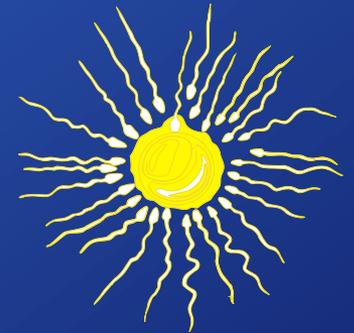
Natural

> 20 million



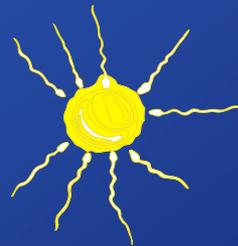
IUI

> 5-10 million



IVF

>1 million



ICSI

1 sperm !



ARTs in Canada

- **No coverage in most provinces**
- In 2010-2015, Quebec was the only jurisdiction in the North American with full coverage of IVF/ICSI.
- **Ontario currently covers 1 cycle of IVF/ICSI in selected couples**
- **Quebec maintains coverage for IUIs**
- **Quebec now covers 1 cycle of IVF/ICSI in selected couples**



Quebec ART Clinical Guidelines - 2015

LES ACTIVITÉS DE PROCRÉATION MÉDICALEMENT ASSISTÉE DÉMARCHE CLINIQUE ET THÉRAPEUTIQUE



10/2015
GUIDE
D'EXERCICE

— Membres du Comité d'élaboration du guide d'exercice sur la procréation médicalement assistée

DR PETER CHAN

Urologue
Centre de reproduction McGill
Centre universitaire de santé McGill

DRE PATRICIA FISCH

Obstétricienne-gynécologue
Centre régional désigné de procréation
assistée
CIUSSS du Saguenay-Lac-St-Jean

DR ROBERT HEMMINGS

Obstétricien-gynécologue
Clinique OVO

DR PIERRE ST-MICHEL

Obstétricien-gynécologue
Clinique Procrea

DRE PAULINE GREF, coordonnatrice

Pédiatre
Adjointe médicale à la direction générale
Collège des médecins du Québec

MME CATHERINE ORDI

Assistante administrative
Collège des médecins du Québec

COLLABORATEURS

DR JOCELYN BÉRUBÉ

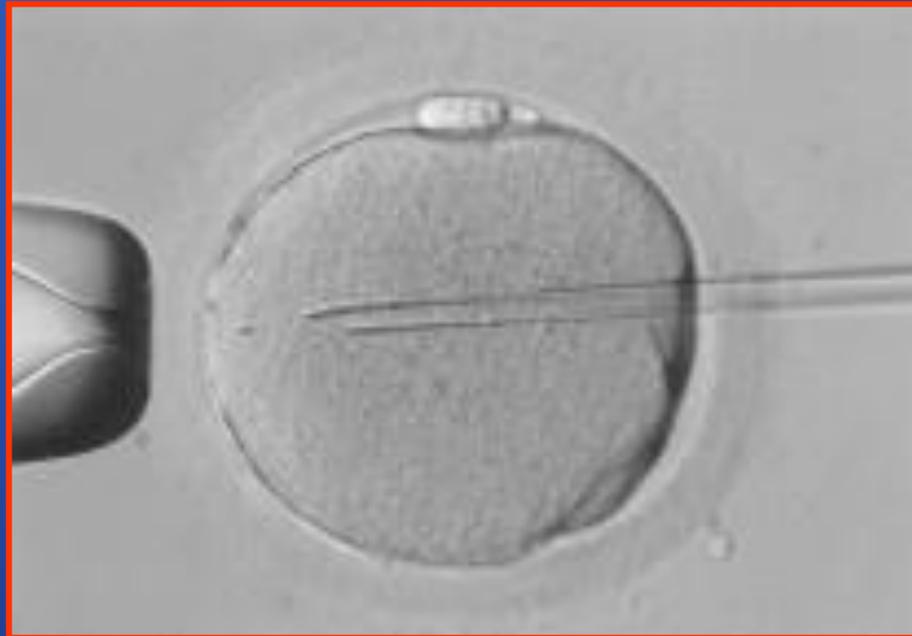
Médecin de famille
Clinique de planning des naissances
de Rimouski
CIUSSS du Bas-St-Laurent

DR ÉLIAS DAHDOUH

Obstétricien-gynécologue
Centre de procréation assistée du CHU
Sainte-Justine
Centre hospitalier universitaire
Sainte-Justine

ICSI: Only 1 Living Sperm is Required!

**WHY BOTHER EVALUATING
THE MEN FOR FERTILITY?**



Epidemiology of Infertility

10% - 15% of couples have fertility problems.



Reasons for Evaluation of Male Fertility

- **>50% of infertility cases are due to male-factor infertility**
 - 33% pure male-factor infertility
 - 33% pure female-factor infertility
 - 33% male- and female-factor infertility



Reasons for Evaluation of Male Fertility

- **Male infertility**

→ **severe underlying illnesses**

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



Reasons for Evaluation of Male Fertility

- Evaluating men is easier than evaluating women
- Should be done before female evaluations:

Scrotum and testes are more assessable than female reproductive organs for evaluations!



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?
- 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



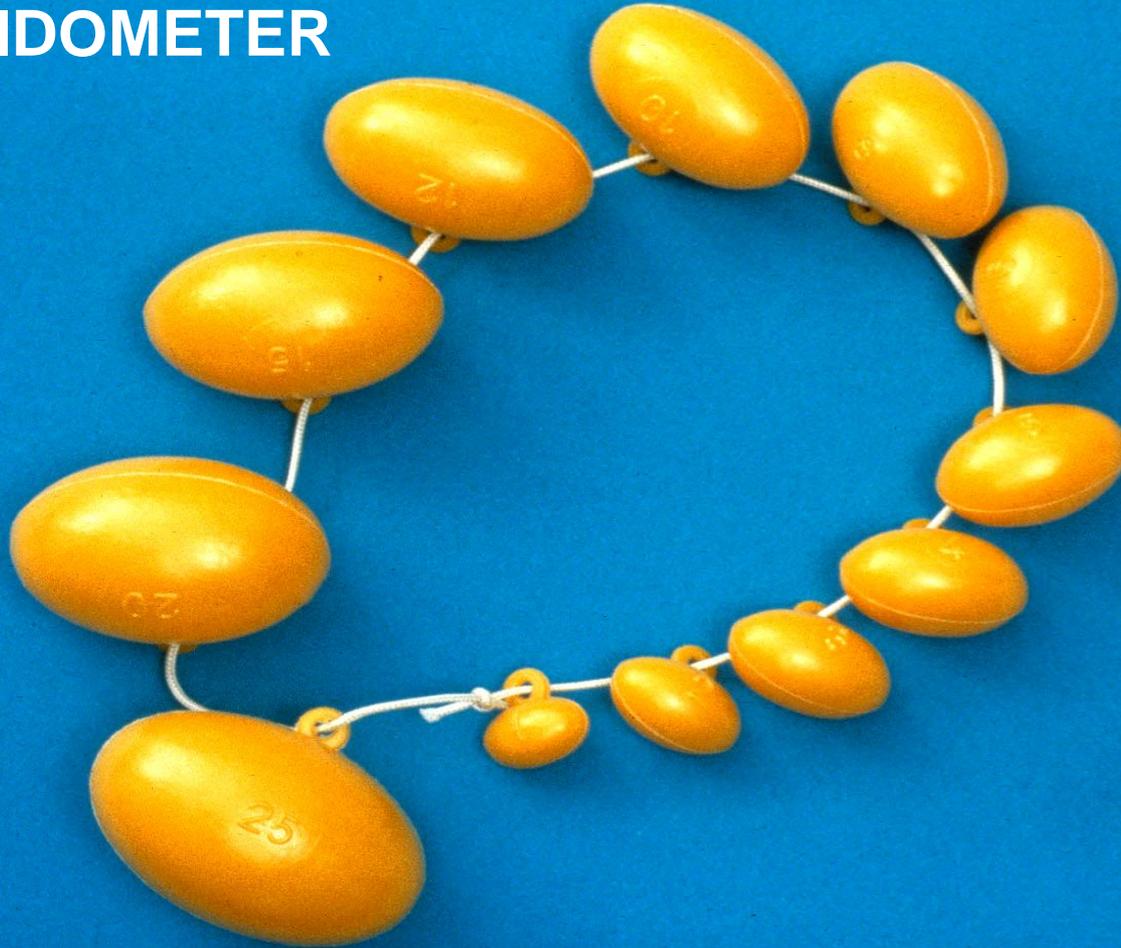
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PHYSICAL EXAMINATION

ORCHIDOMETER



PHYSICAL EXAMINATION

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

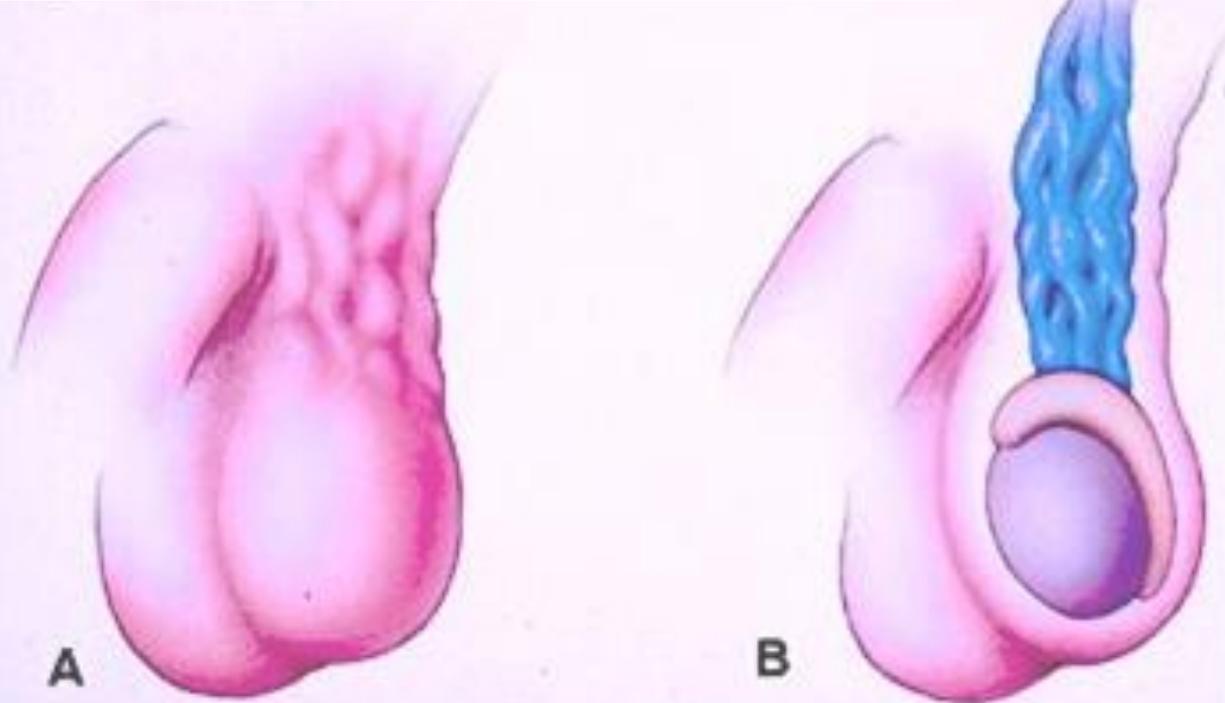
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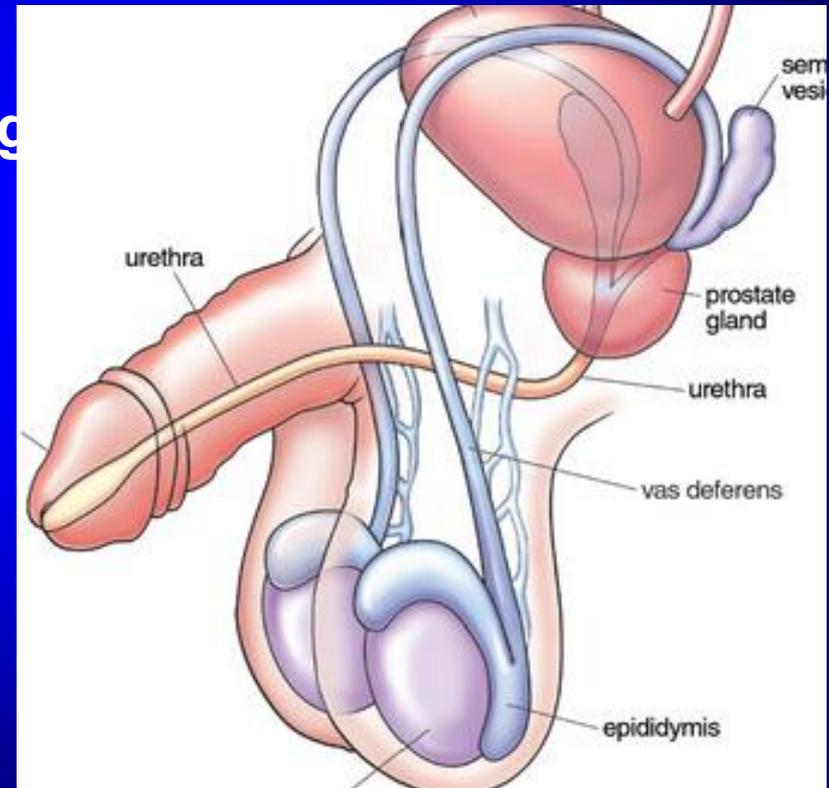
Varicoceles

“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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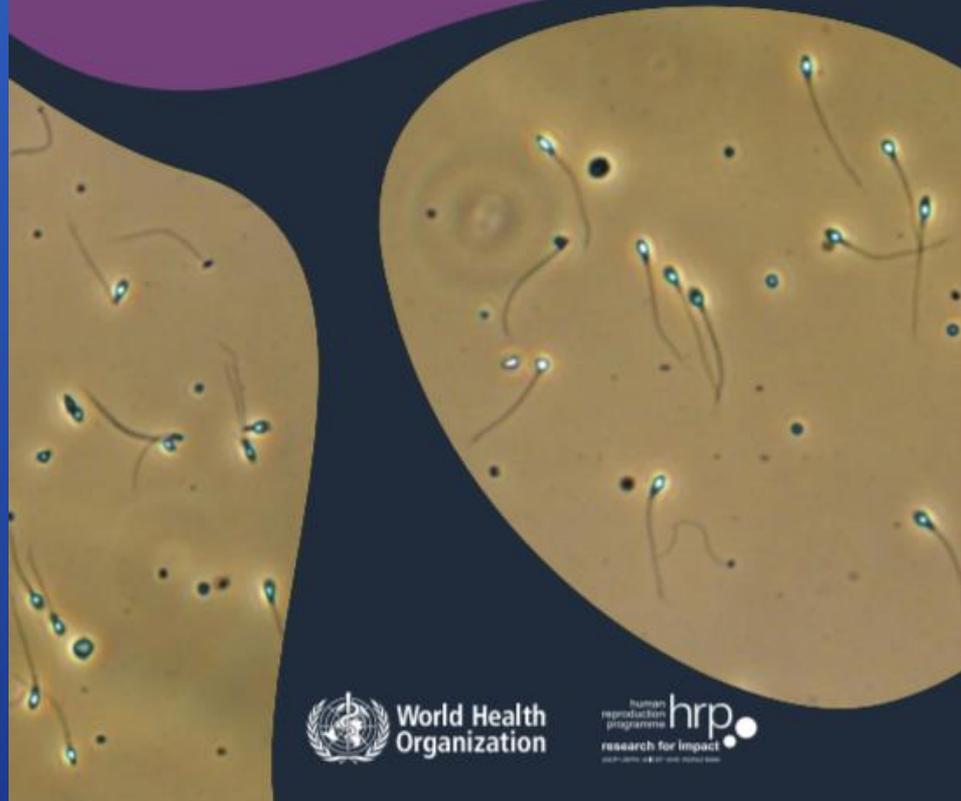
SEMEN ANALYSES

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



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

Sixth Edition



Semen analysis – reference values

Volume:	> 1.4 ml
pH:	≥ 7.2
Sperm count:	> 16×10^6 / ml
Total count:	> 39×10^6
Progressive Motility:	> 30%
Morphology:	>4%



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



INTERPRETATION OF SEMEN ANALYSIS

- Common mistake → No work-up needed if semen parameters meet the reference values
- Bypassing male fertility work-up → Dangerous for the male partners
- Bypassing male fertility work-up → Unnecessary risks and burdens on female partners
- Bypassing male fertility work-up → Unnecessary use of ARTs

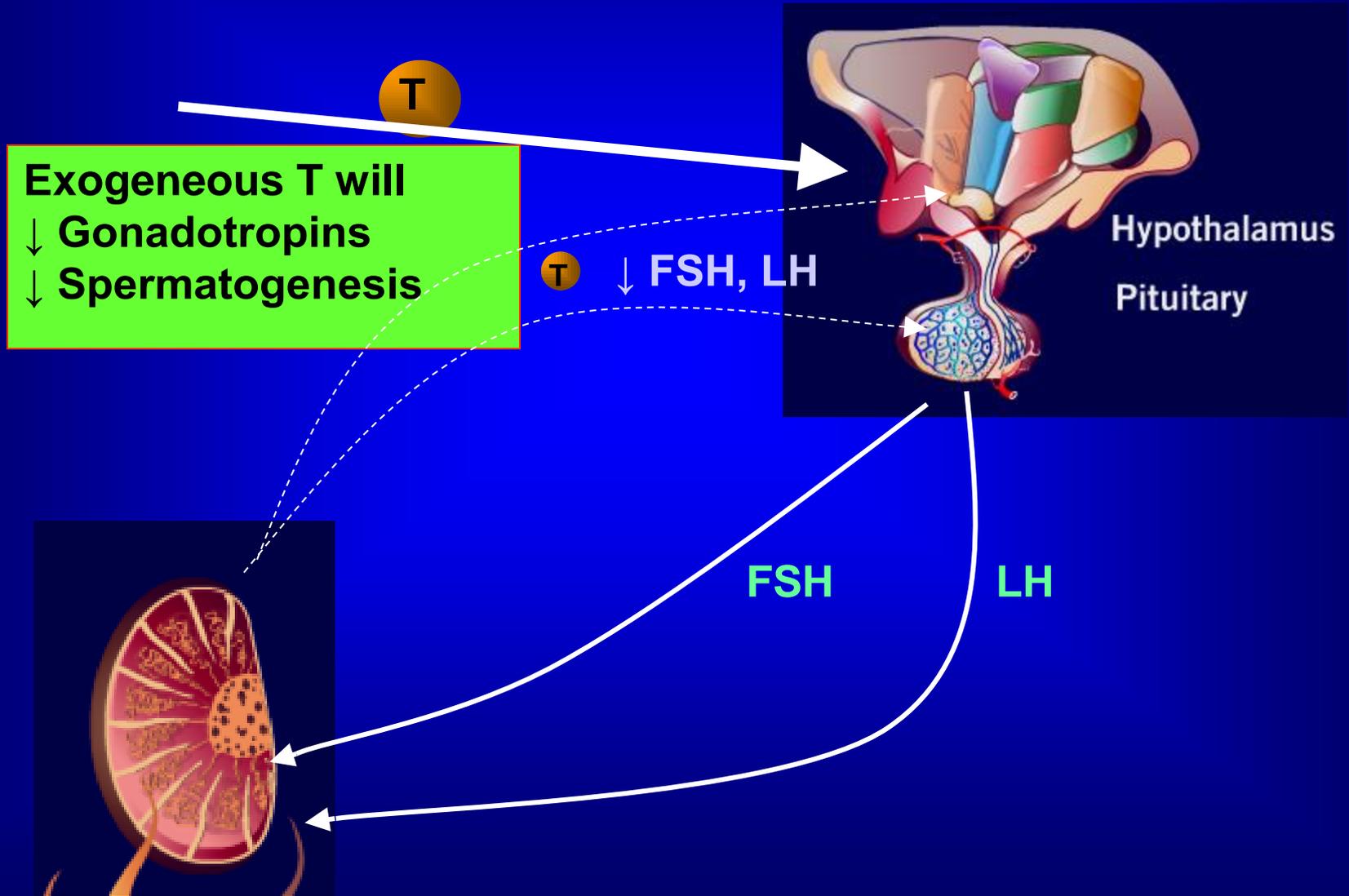


HORMONAL EVALUATION

- NOT all men needs hormonal evaluation upfront
- [sperm] < 10 million/ml
Sexual dysfunction
Other symptoms or signs suggesting endocrinopathies
- Morning total T and FSH
LH, bio-available T, estradiol, prolactin (if hypogonadal)
TSH if clinical thyroid dysfunction



WHY NOT JUST GIVE THEM TESTOSTERONE?



Common Genetic Tests for Male Infertility

- **Group I: Chromosomal disorders**
 - Klinefelter's syndrome (47 XXY)
 - Structural abnormalities of chromosomes (deletion, duplication, inversion, translocation)
 - Karyotype
- **Group II: Microdeletion of Y-chromosome**
 - PCR-based test
- **Group III: Single gene disorders**
 - Cystic fibrosis
 - CFTR gene mutation screening



Y-Chromosome

- It was considered a “genetic wasteland” ~50 yrs ago.
- Small size with only a few genes.
- Half of the population do not even have one. (or need one!)



Y-Chromosome Microdeletion: Clinical Significance

- Y-chromosome microdeletion results in severe impairment in spermatogenesis
- Most frequently identifiable genetic cause of infertility
- ARTs likely needed for reproduction
- Male offspring will inherit the Y-chromosome
- Genetic counseling is crucial

Hopps CV, et al. *Hum Reprod.* 2003;18:1660-1665.



Peter Chan M.D.

CUA Guideline: The workup and management of azoospermic males

Keith Jarvi, MD, FRCSC; Kirk Lo, MD, FRCSC;* Ethan Grober, MD;* Victor Mak, MD, FRCSC;* Anthony Fischer, MD, FRCSC;† John Grantmyre, MD, FRCSC;‡ Armand Zini, MD, FRCSC;‡ Peter Chan, MD, FRCSC;‡ Genevieve Patry, MD, FRCSC;‡ Victor Chow, MD, FRCSC;§ Trustin Domes, MD, FRCSC#*

*Department of Urology, Mount Sinai Hospital, University of Toronto, Toronto, ON; †Division of Urology, McMaster University, Hamilton, ON; ‡Department of Urology, Dalhousie University, Halifax, NS; †Division of Urology, McGill University Health Centre, Montreal, QC; ‡Hôtel-Dieu De Lévis, Lévis, QC; §Department of Urologic Sciences, University of British Columbia, Vancouver, BC; #Saskatoon Health Region, Saskatoon, SK

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Published online August 10, 2015.

A committee was established at the request of the Canadian Urological Association to develop guidelines for the investigation and management of azoospermia. Members of the committee, all of whom have special expertise in the investigation and management of male infertility, were chosen from different communities across Canada. The members represent different practices in different communities.

Introduction and background

Infertility or subfertility affects 15% of couples in Canada, with a male factor contributing to the fertility problem in close to 50% of these couples. Of the men presenting for fertility investigation, up to 20% are found to be azoosper-

A further group of men have a failure to ejaculate. These may be men with spinal cord injury, psychogenic failure to ejaculate, or neurological damage (sympathetic nerve damage from, for example, a retroperitoneal lymph node dissection).

To understand the management of azoospermia, it is important to also understand the role of assisted reproductive technologies (ARTs) (i.e., in-vitro fertilization) in the treatment of azoospermia. Since the 1970s, breakthroughs in the ARTs have allowed us to offer potentially successful treatments for up to 98% of couples with male factor infertility.⁶ These significant advances had little to do with techniques to improve the sperm quality, but relied on the use of ARTs to “treat” the male infertility. These programs used techniques to increase the number of mature eggs produced by the women by manipulating the hormonal environment in the women using exogenous hormones (ovulation induction) then used either:

AZOOSPERMIA

- Worst case scenario
- Is there an obstruction (Obstructive azoospermia)
- Or testicular dysfunction (Non-obstructive azoospermia)



Causes of azoospermia

OBSTRUCTIVE AZOOSPERMIA (Normal sperm production)

Post-vasectomy

Epididymitis (STD's)

Hernia surgery (bilateral)

Scrotal surgery

Bilateral absence of vas

NON-OBSTRUCTIVE AZOOSPERMIA (↓ sperm production)

Undescended testes

Post- chemotherapy

Mumps orchitis (post-pubertal)

Klinefelter's syndrome

Y-chromosome microdeletion

Hypogonadism

Discussion – what do you expect?

OBSTRUCTIVE AZOOSPERMIA (Normal sperm production)

Testis size and texture are full, epididymides full

Normal testosterone

FSH low normal

NON-OBSTRUCTIVE AZOOSPERMIA (↓ sperm production)

Small size and soft testes, flat epididymides

Testosterone normal or low

Elevated FSH

Management

OBSTRUCTIVE AZOOSPERMIA (Normal sperm production)

If vas deferens absent may consider CFTR genetic test

High probability of finding sperm by aspiration for ICSI

Some cases may be feasible for microsurgical reconstruction

NON-OBSTRUCTIVE AZOOSPERMIA (↓ sperm production)

Genetic testing with karyotype and Y-chrom microdeletion

Chance of finding sperm for ICSI at best 50-60%

May need to consider using donor sperm

Summary

- Male factor infertility is common among infertile couples
- Male infertility may be associated with underlying significant co-morbidities
- With the introduction of IVF coverage in QC, more patients may request fertility evaluation
- A thorough male infertility investigation can be conducted in the office setting for most infertile couples

