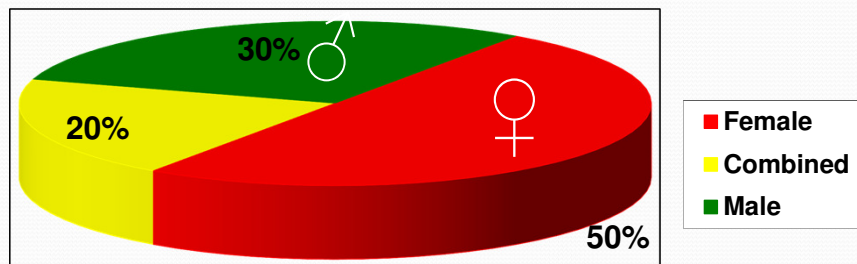


## Infertility, Assisted Human Reproduction and the Family Physician - Male Infertility

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### Contributors to Infertility



## ART - ICSI

### *Introduction*

Investigation of the male is mandatory in a subfertile couple for

Disease Detection

Disease Prevention

Treatment of Male Infertility

## Disease Detection

- Cryptorchidism
  - Incidence at birth ~3-4%
  - Incidence in adulthood 0.7-0.8%
  - ~ 6% of Male Infertility will be caused by cryptorchidism

## Disease Detection

Testis Tumour in the population of subfertile men is  
~20X the norm

Raman, Nobert, Goldstein, J Urol 174(5), 2005.

## Disease Detection

Male Infertility Associated with at least a 2x higher risk  
of **high grade** prostate cancer

Walsh et al. Cancer. Epub. March 2010

## Disease Detection

Other Significant Conditions:

Pituitary Tumours  
Thyroid Abnormalities  
Diabetes  
Cystic Fibrosis

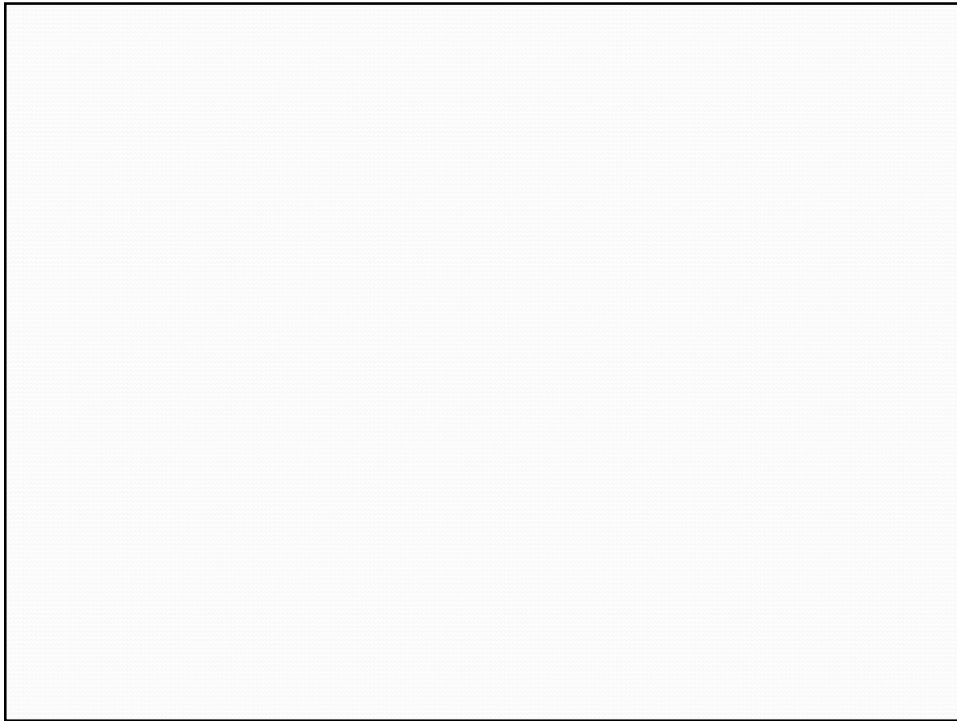
Any significant illness.....

## Disease Detection Genetic Considerations

- Abnormalities in Chromosome Numbers (Aneuploidy)
- Abnormalities in Chromosome Structure (Translocations/Deletions)
- Specific Gene Abnormalities

## *Genetic Considerations*

	<i>Azospemia</i>	<i>Severe Oligospermia</i>
<i>Sex Chromosome</i>	XXY – 10% Other 2%	2%
<i>Autosome</i>	1%	3%
<i>Overall</i>	13%	5%



## Genetic Considerations

Rate of Balanced Translocations - 8X normal males (  $\frac{1}{2}$  B/W 13 & 14)

Typically few viable pregnancies, but potentially could produce viable embryo

## *Y-microdeletion and Male Infertility*

## *Cystic Fibrosis and Male Infertility*

1969 – Cystic Fibrosis men azospermic, all CBAVD

1988 – CBAVD → IVF

## *Cystic Fibrosis and Male Infertility*

Cystic Fibrosis transmembrane conductance  
regulator gene (CFTR) chromosome 7

### Cystic Fibrosis

Autosomal recessive disorder

Carrier Status	1 in 25 (of general population)
Cystic fibrosis	1 in 2500

## *Cystic Fibrosis and Male Infertility*

If cystic fibrosis heterozygous or homozygous detected in a  
male, it is mandatory that his female partner be screened  
as well!



## Treatment for Male Infertility

### Varicoceles

Most Common cause of Male Infertility

General Prevalence	15%
Primary Infertility	~30%
Secondary Infertility	50-70%

## Varicoceles

Preponderance of Clinical and Animal Models show deleterious effect on spermatogenesis

## Varicoceles

? Role of Varicocelectomy in the age of Assisted Reproductive Technology ?

## Varicoceles

1. Significantly more cost effective than ART
2. Can improve success rates of ART
  - Daitch et al, Journal of Urology 2001  
Varicocelectomy and IUI

	% Untreated	% Treated
Preg/cycle	6.3	11.8
Live Birth/cycle	2.1	11.8
Live Birth/couple	4.2	32.4

## Varicoceles

3. May change the type of ART required  
i.e. IVF → IUI      ICSI → IVF
4. May change the need for sperm retrieval  
may change NOA to oligospermia

## Varicoceles

### Take Home Message

1. Varicoceles are common and are associated with subfertility
2. Varicocelectomy will improve semen parameters in 60-70%
3. Pregnancy rates in order of 30-50%
4. May change treatment even if ART is required

## Lifestyle Issues

- Smoking
- Recreational drugs
  - Marijuana, Alcohol, Cocaine
- Weight, nutrition and exercise
- Cell phones
- Caffeine
- Heat and tight clothes

## Male Fertility

- 37 y/o male with 1 year of primary infertility
  - Smokes 1 PPD
  - ETOH 3 daily
  - Coffee 2-3 cups daily
  - Occasional Marijuana
  - Wears cell phone at the hip

## Smoking: Semen Parameters

- Semen Parameters in men exposed in utero to cigarette smoke
  - Decreased sperm density, motility and normal morphology
  - Decrease of 19% in sperm density

## Smoking: Semen Parameters

- Semen Parameters
  - Most studies show: Decreased sperm **density**, **motility and normal morphology**
  - Decrease of 22% in sperm density in infertile men
  - Large series (2542 men) of normal men:
    - 19% reduced sperm concentration
    - ? Dose effect

Marinelli 2007  
Marino 1998  
Al Bader et al 1999

## Smoking: Semen Parameters

- Smoking associated with increase DNA fragmentation
- Longer TTP (54% higher in couples with male smokers)
- Reduced Fertilization rates at IVF
- ? Higher rates of birth defects
  - Confounder is the impact of second hand smoke

## Alcohol and Male Infertility

- Alcoholics:
  - 75% have testis atrophy
  - Acute use of ETOH reduces testosterone
- Moderate alcohol use
  - Protective effect! May be related to red wine and antioxidant effects
- Heavy alcohol use
  - Sparse data
  - Rats: decreased litter size and birth weight

## Male Fertility: Marijuana

- Marijuana:
  - 11% of those 16-59 use marijuana
  - Cannabinoid receptors found in testis, vas deferens and sperm
  - In sea urchin, these receptors mediate inhibition of the acrosome Rxn
  - High dose use of Marijuana (> 8 cigs/day) resulted in decreased counts, motility, normal morphology
  - Incubating sperm with THC results in decreased motility, slower sperm and less linearity, as well as reduced acrosome rxn
  - No change in hormone levels
  - **Marijuana might have an impact on sperm function critical for fertilization**

Whan 2006

## Weight and Exercise

- The incidence of oligozoospermia and asthenospermia
  - 5.3% and 4.5% in normal-weight men
  - 9.5% and 8.9% in overweight men and
  - 15.6% and 13.3% among obese men
- Likely causes
  - Increased conversion of T to estrogen
  - Higher heat around the testis
    - **The Practice Committee of the American Society for Reproductive Medicine 2008**

## Cell Phones and Male Infertility

- Study found inverse correlation with the percent of morphologically normal sperm and cell phone use in infertile men
- In-vitro study exposing human sperm to cell phones:
  - RF-EMW showed a significant decrease in sperm motility and viability, increase in ROS levels
  - Suggested keeping cell phones away from pelvis

Wdowiak 2007  
Agarwal 2009



## Male Fertility: Cell Phones

- Sparse evidence
- May suggest moving cell phone away from groin

## Caffeine and Male Infertility

- Caffeine used in-vitro to stimulate sperm motility
- Does caffeine have any adverse impact on male reproductive function?
  - Caffeine reportedly inhibits DNA repair mechanism
- Unable to find any literature to support a negative impact of caffeine on male fertility

## Male Fertility; Tight underwear

- Risk of abnormal s/a is doubled if the man regularly wears tight underwear or tight trousers
- Tight underwear have been used as a contraceptive

Parazzini, F 1995

## Scrotal Heating and Male Infertility

- Testis are temperature sensitive (most sensitive cells are the pachytene sp)
- Heat stress induces apoptosis
- Cooling improves spermatogenesis

Jung 2007

## Heat

- Sources of heat
  - Prolonged sitting
  - Sitting on heated floor, car seat
  - Professional drivers
    - {reduced semen parameters}
  - Sauna and water bath
  - Tight underwear: {reduced semen parameters}
  - Fever: {reduced semen parameters}

## Scrotal Cooling

Improvements in sperm

Parameters with cooling

- 7X in one series: ice packs  
(Davidson 1954)
- 66% improved: evaporation device  
(Zorgniotti 1980)
- Up to double sperm counts: cool air  
stream at night (Jung 2001)

## *Conclusion*

Investigation of the male is mandatory in a subfertile couple for

Disease Detection

Disease Prevention

Treatment of Male Infertility