

**11th Postgraduate Course for Training in
Reproductive Medicine and Reproductive Biology**

**MALE INFERTILITY AND
ENVIRONMENTAL FACTORS**

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MALE INFERTILITY AND ENVIRONMENTAL FACTORS

INTRODUCTION

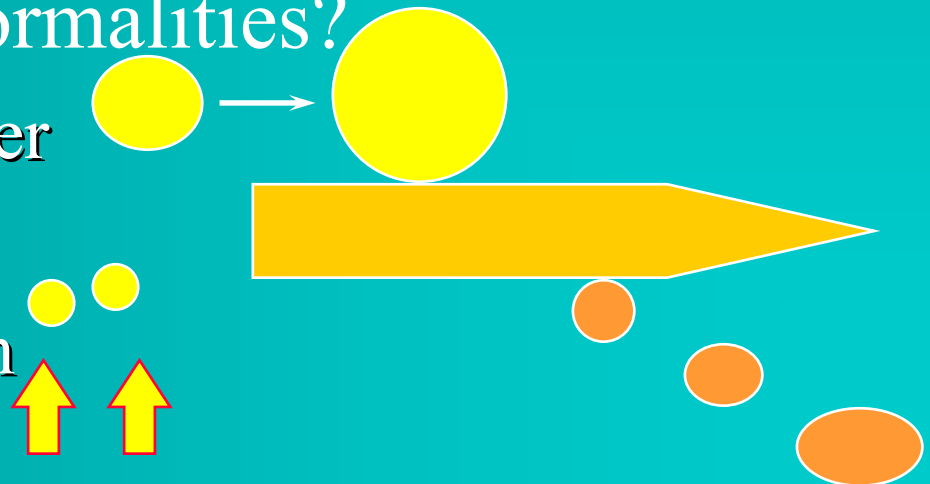
- environmental influences on reproductive function in human male
 - diet
 - lifestyle
 - occupational life
 - diseases patterns
 - environmental factors
man-made chemicals
 - contamination with

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RESULTS

- declining male reproductive health?
- decreasing semen quality?
- increasing testicular cancer and urogenital abnormalities?

- testicular cancer
- hypospadias
- cryptorchidism



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RESULTS

- poor efficiency of spermatogenesis
- high proportion of morphologically abnormal sperm (50% or more)
- naturally great variation in semen quality
 - between individuals
 - from ejaculate to ejaculate in the same individual
- evolutionary origin of human (non-seasonal breeder)

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RESULTS

- to detect a small effect on male fertility:
requires large numbers of samples
 - age
 - occupation
 - reproductive status/history
 - variation in exposure to the agent
 - geography
 - behaviours
- studies extremely -laborious, -expensive,

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RESULTS

- it is not possible to conclude definitely that human MSC has declined during the last 100 years



- large amount of confounding factors might have an influence on human male reproductive health

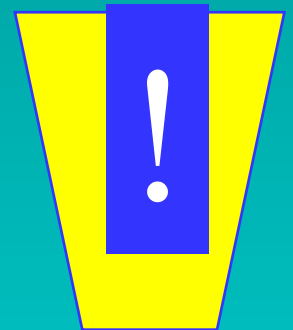
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RESULTS

- substantial change in diseases patterns
much longer live

- therapeutic drug intake -lifestyle
- environmental factors - dietary

more important

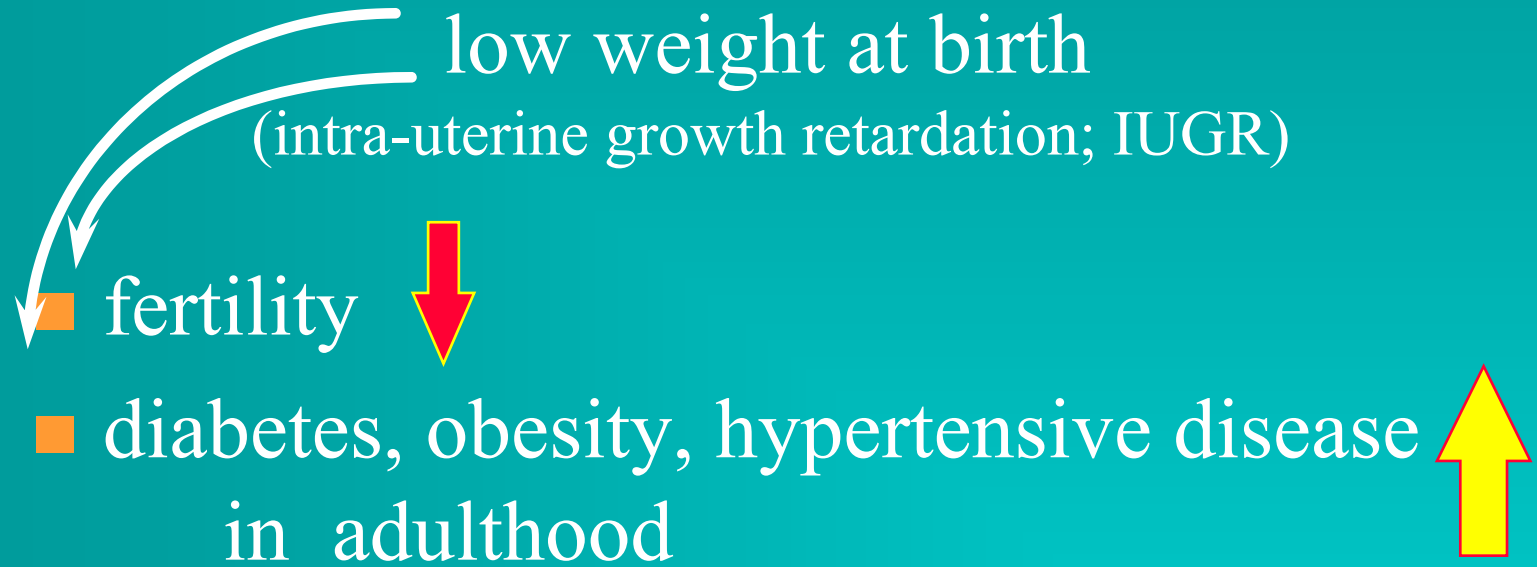


- important disorders in adulthood

may be altered by environmental/lifestyle factors acting during fetal life or early infancy

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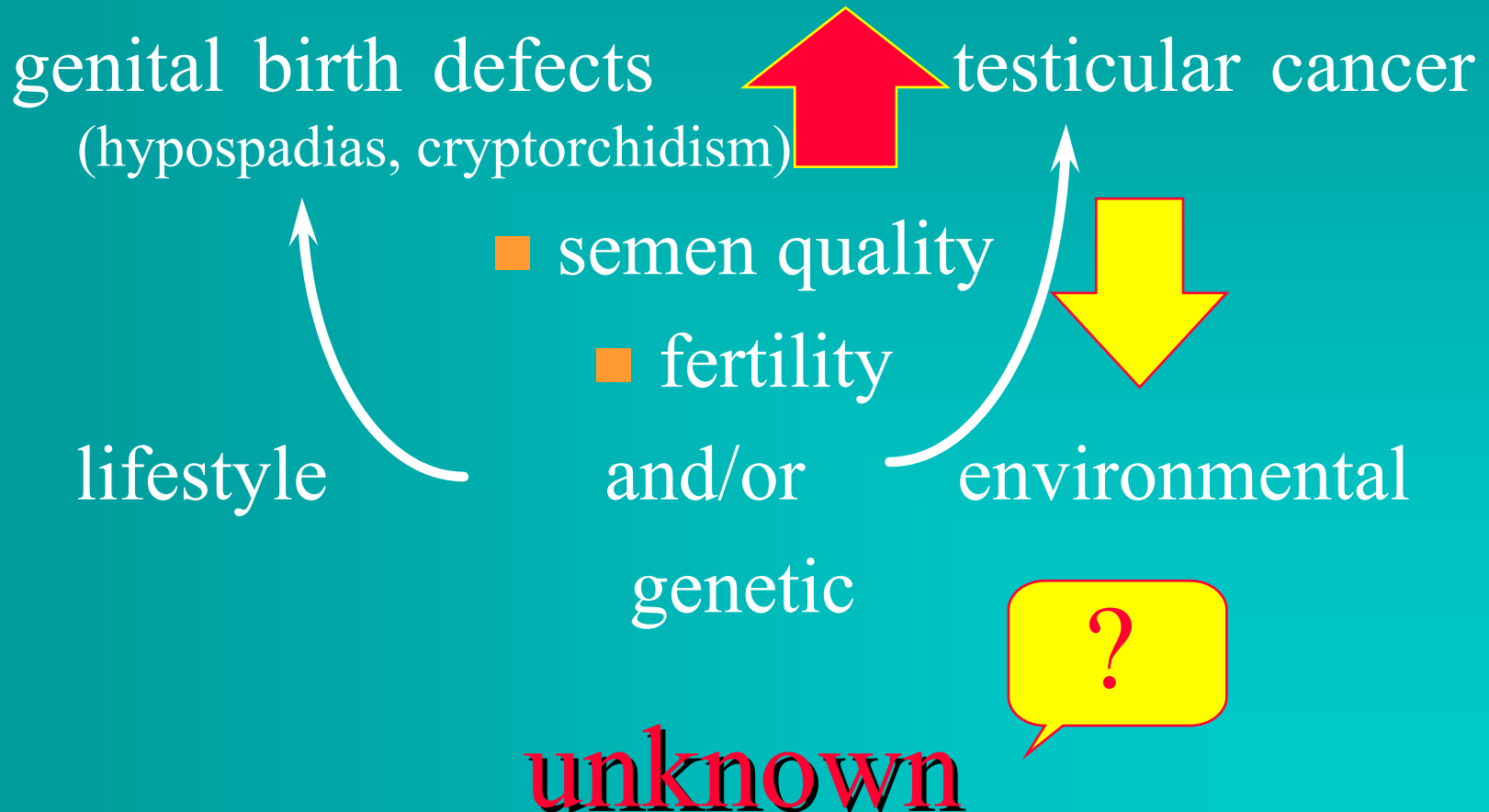
RESULTS



fetal- and neonatal life is important in
development of reproductive disorders

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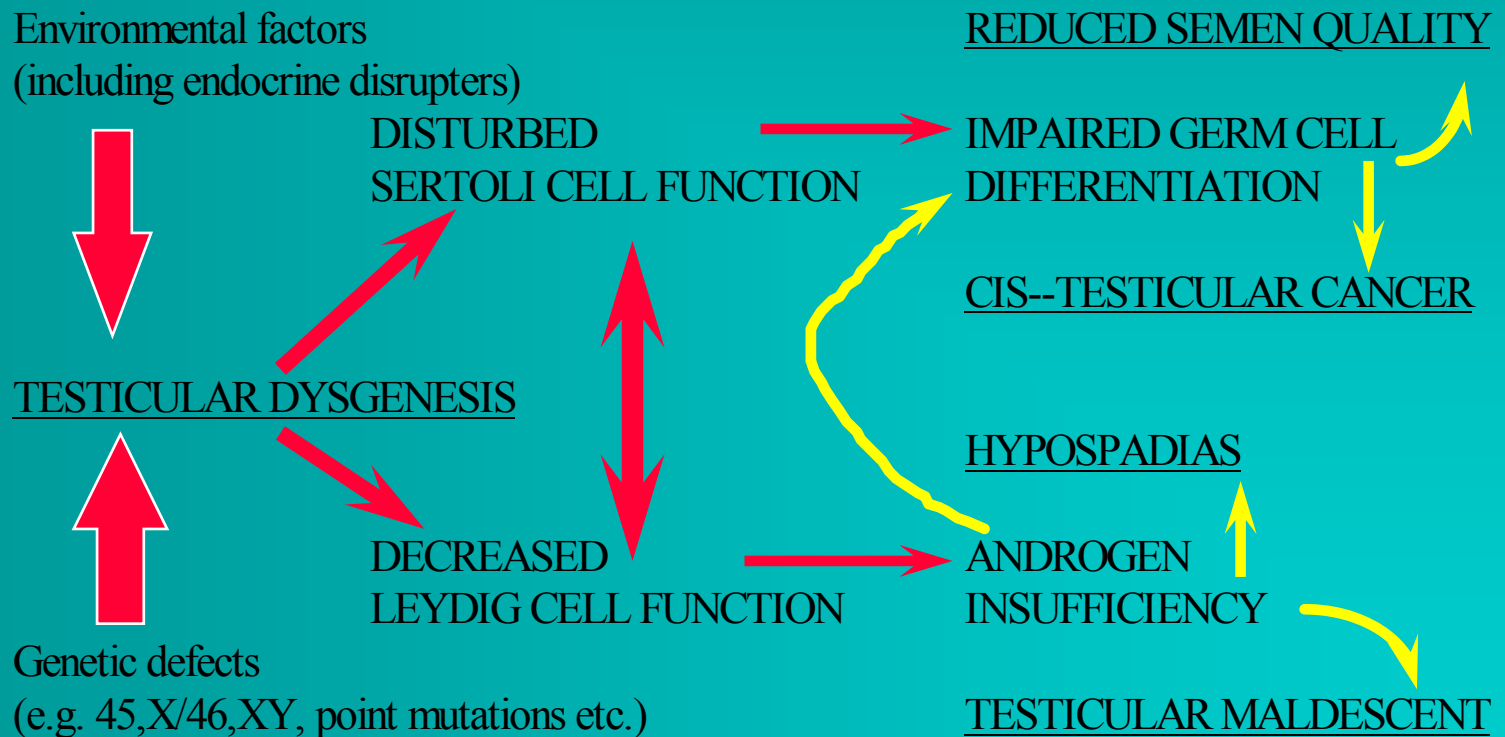
RESULTS



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RESULTS

Schematic representation of pathogenetic links between the components and clinical manifestations of **testicular dysgenesis syndrome**

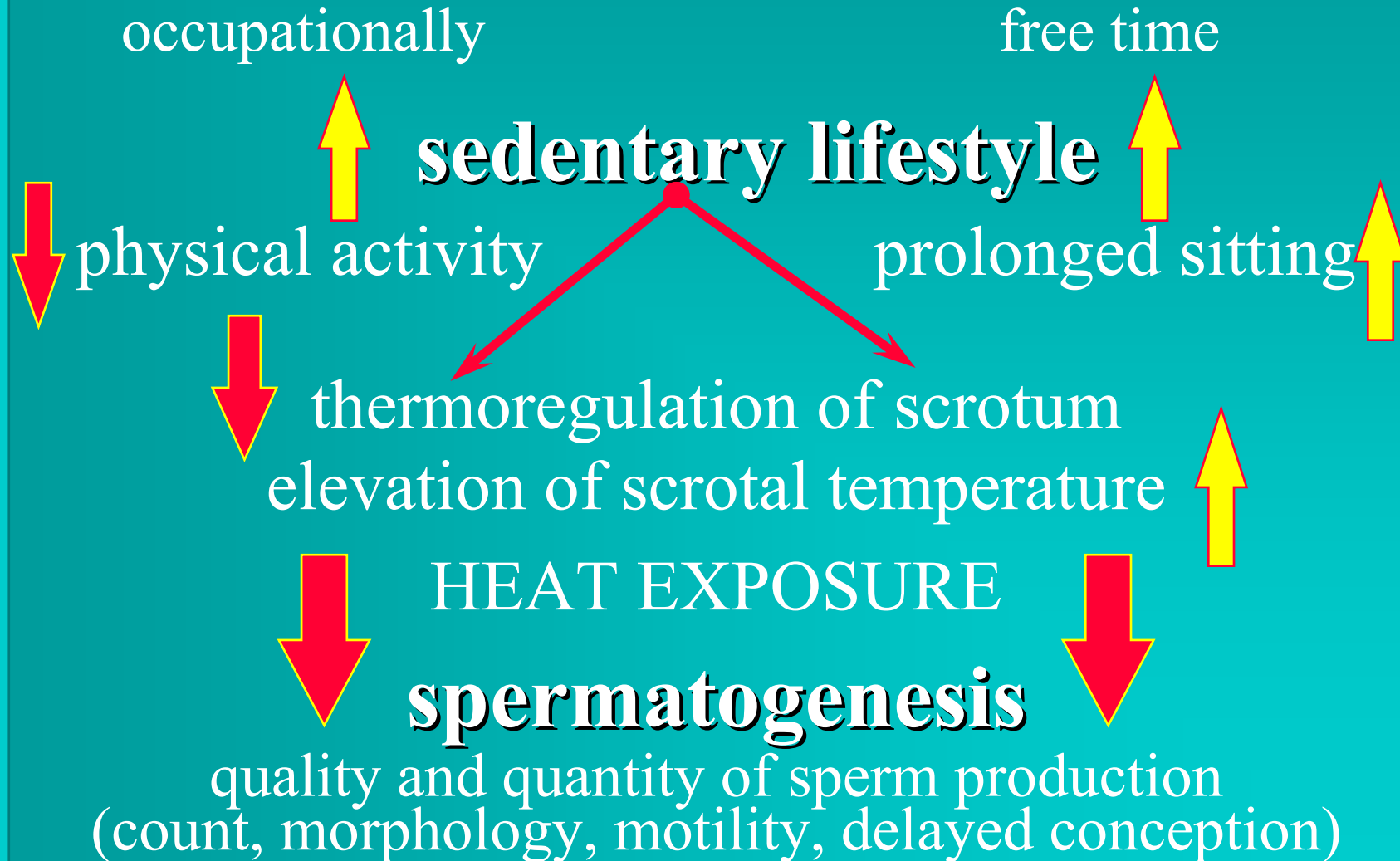


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MALE INFERTILITY AND ENVIRONMENTAL FACTORS

RESULTS



MALE INFERTILITY AND ENVIRONMENTAL FACTORS

RESULTS

- the mean scrotal temperatures are higher in infertile men (are higher in infertile men with varicocele)
- abnormalities in spermatogenesis are reversible when the hyperthermic action is stopped
- the magnitude of the effect of elevated scrotal temperature on semen parameters is both temperature- and time-dependent

scrotal heating, might be a contributory factor to the high rate of early pregnancy loss in the human by altering DNA integrity of the sperm

aluminium

submarine

nocturnal cooling

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RESULTS

seasonal changes

human sperm counts and/or semen qualities are consistently poorer in the summer than winter
30% reduction no variation

currently no consensus to fertility

it can be argued that because there is a similar fall in summer sperm counts in men from both temperate and more equatorial regions, then heat is unlikely to be the key factor

a residual seasonal effect?
(a universal underlying cause)

MALE INFERTILITY AND ENVIRONMENTAL FACTORS RESULTS



hormonal

EXPOSURE

chemical



hormonally active

effective as **endocrine disruptors**

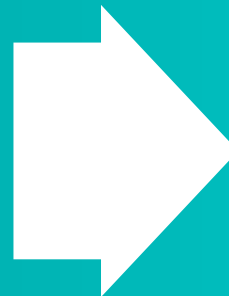
oestrogenic and/or anti-androgenic activity



fetal life or early infancy

adulthood

- genital birth defects
- testicular cancer
- breast cancer



- semen quality
- semen quantity
- fertility ?**



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Potential mechanism for effect on sperm production/fertility: I.

- Exposure to pesticides:

 - More intensive agriculture

 - Introduction and expanded use of pesticides

 - Modern pesticides are probably far safer than those in use 20 years ago

 - Increased consumption of animal fats may deliver a cocktail of fat-soluble chemicals

- Exposure to other chemicals:

 - Greater time spent driving and in traffic queues

 - Increased atmospheric pollution

 - Increased chemical contaminants in drinking water

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Potential mechanism for effect on sperm production/fertility: II.

- Altered hormonal exposure:

Dietary changes may alter metabolism of endogenous hormones

Consumption of meat from hormone treated livestock

(hormone residues in fat)

Increased consumption of soy-containing products

Increased exposure to environmental hormones via food packaging and greater use of pre-packaged foods

- Recreational/ performance-enhancing drugs:

Increase in use of recreational drugs

Body-image concerns have led to increased use of anabolic steroids, etc.

- Therapeutic treatments:

Antibiotics or other widely prescribed drugs and cancer therapy may adversely affect spermatogenesis

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Principal exogenous substances that may affect sex hormone function I.

Oestrogenic and anti-oestrogenic effects !

- 1-High potency :
 - Diethylstilbestrol (DES)
 - Ethinyl oestradiol (component of contraceptive pill)
- 2-Medium potency
 - Phyto-oestrogens, *isoflavones (for example genistein, daidzein), *coumestans (for example coumestrol), *lignans
- 3-Low potency
 - Bisphenol A
 - Octylphenol and nonylphenol
 - Pesticides, including chlordecone, DDT, dieldrin, endosulfan, p,p'-methoxychlor, toxaphene

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Principal exogenous substances that may affect sex hormone function II.

Anti-androgenic effects !

- p,p'-DDE
- Certain phthalates (for example DBP, DEHP)
- Pesticides, including linuran, procymidone, metabolites of vinclozilin
- Hyhydroxyflutamide

Others

- Dioxins, furans, and dioxin-like PCBs (polychlorinated biphenyls)

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DISCUSSION

- the impact of environmental exposures on fertility and its long-term preservation in the human male are not established
- chronic exposures to reproductive toxins are not well documented
- mechanisms of toxicity are either poorly understood or unknown
- the increase, year by year, in incidence of testicular cancer in the world is established

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DISCUSSION

The factors which may influence the sperm count and explain part of the variability:

- Those linked to the characteristics of the men included in the study,
- Those depending on the methodologies used to analyse the semen or the data,
- Those depending on external factors influencing sperm production.

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DISCUSSION

- It is necessary to conduct well defined; multi centre prospective studies of men in various population categories.
- These studies should take into account other factors, which may interfere with male reproductive health and include other sperm characteristics, which may be better biomarkers of testicular function and human fertility.
- When the influence of confounding factors is available, this should be taken into account in the statistical analysis in order to better compare data from various centres or times.

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