The University Of Sheffield.

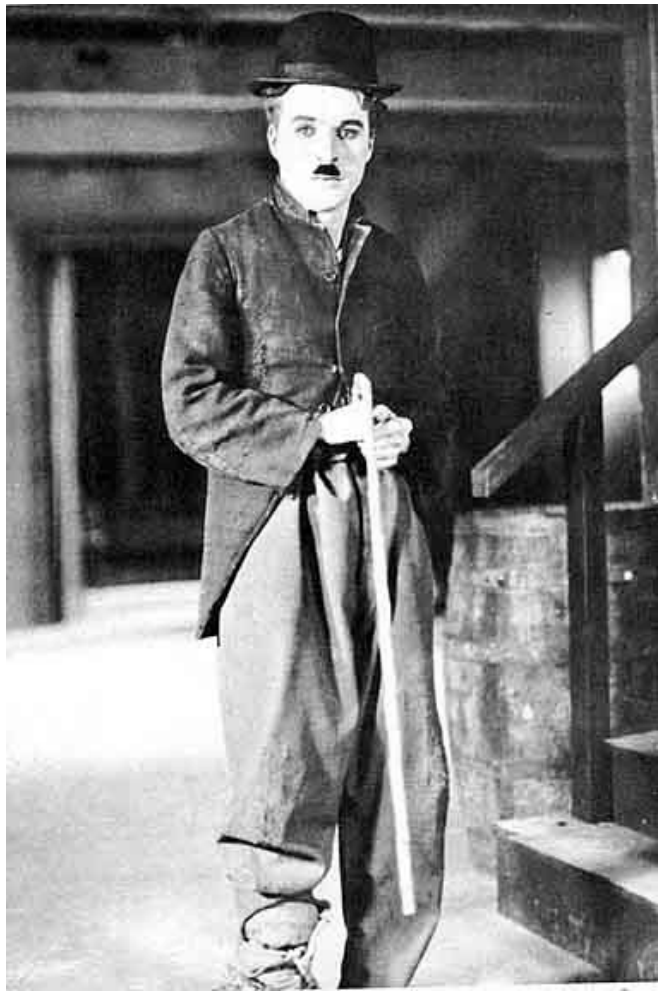
Male fertility and infertility

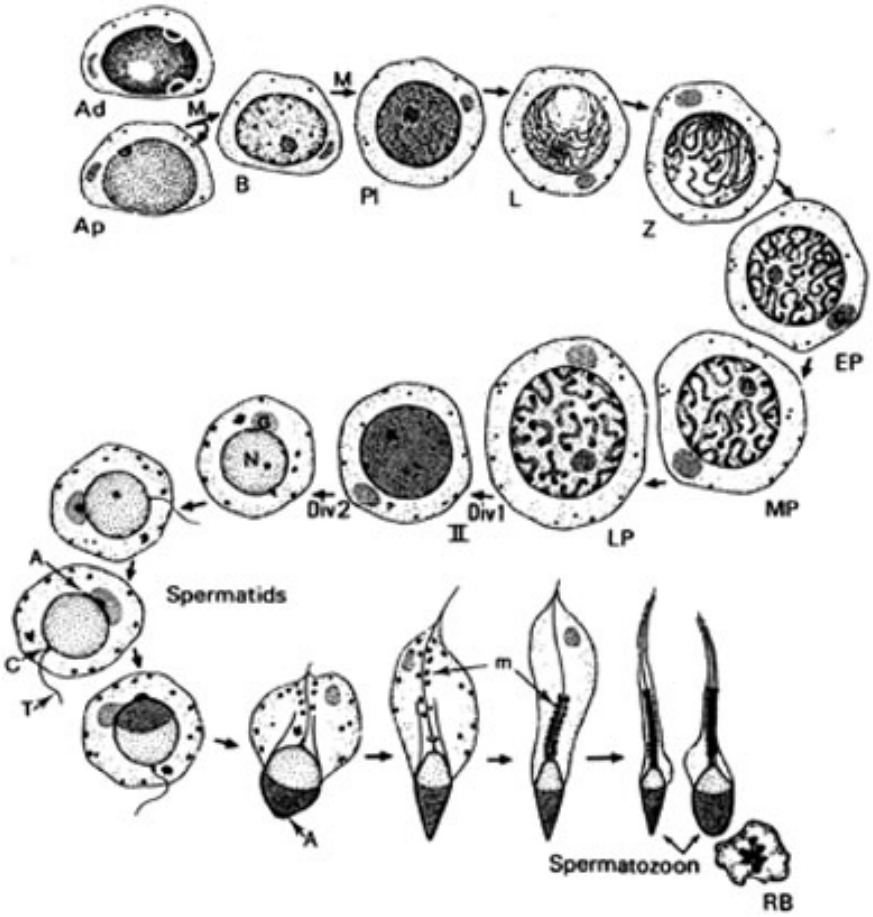
Allan Pacey
University of Sheffield
Sheffield Teaching Hospitals

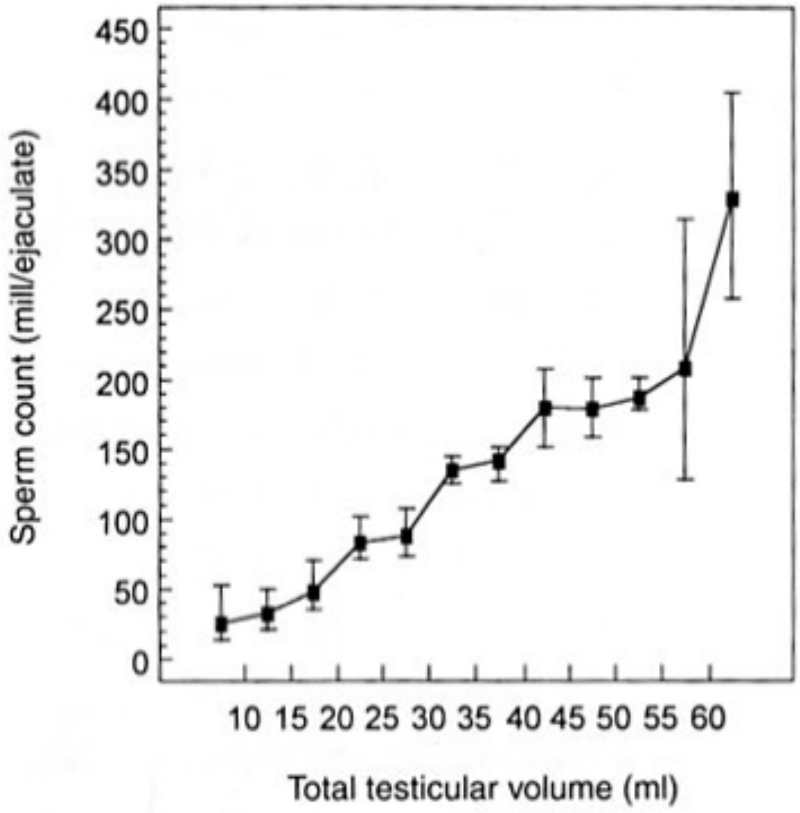
The University Of Sheffield.

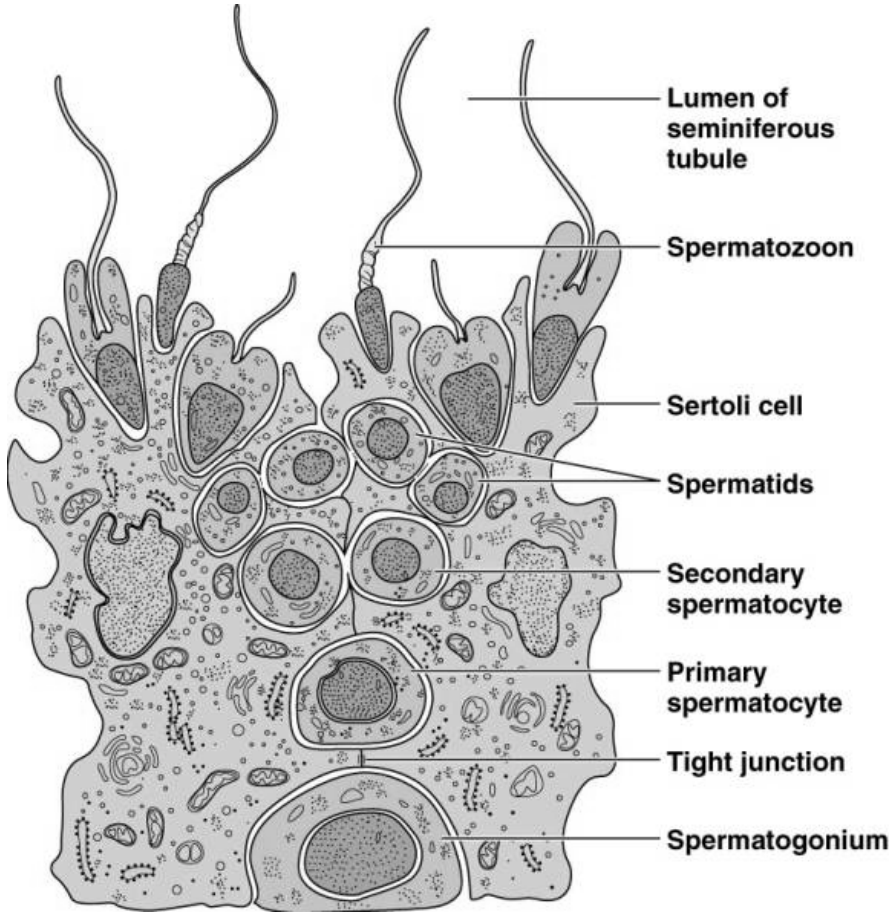
A.Pacey@Sheffield.ac.uk
http://www.twitter.com/allanpacey

Background to male fertility



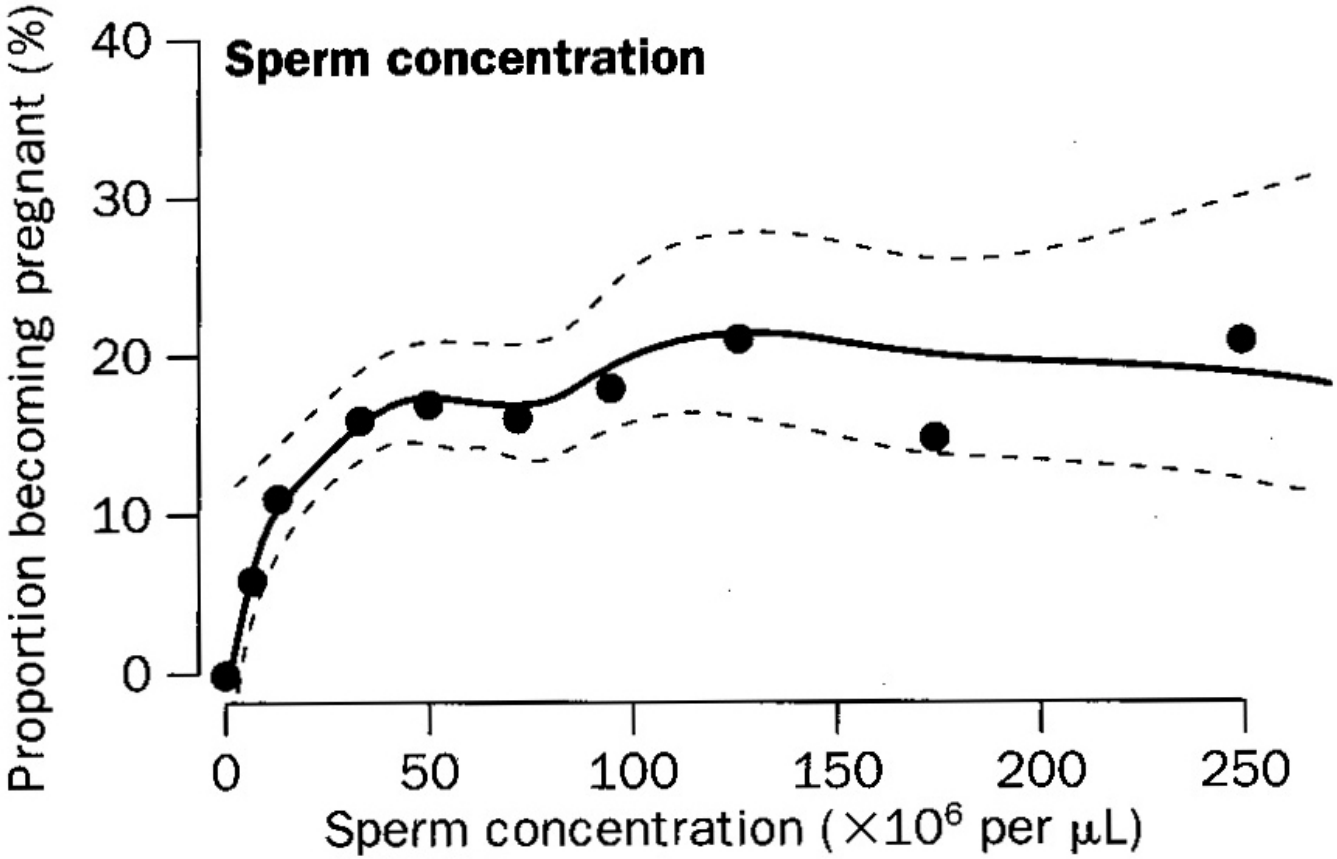

Ad
Ap
M
M
B
Pl
L
Z
EP
MP
LP
II
Div1
Div2
N
A
C
T
Spermatids
m
A
Spermatozoon
RB





WHO (2000) Cambridge University Press

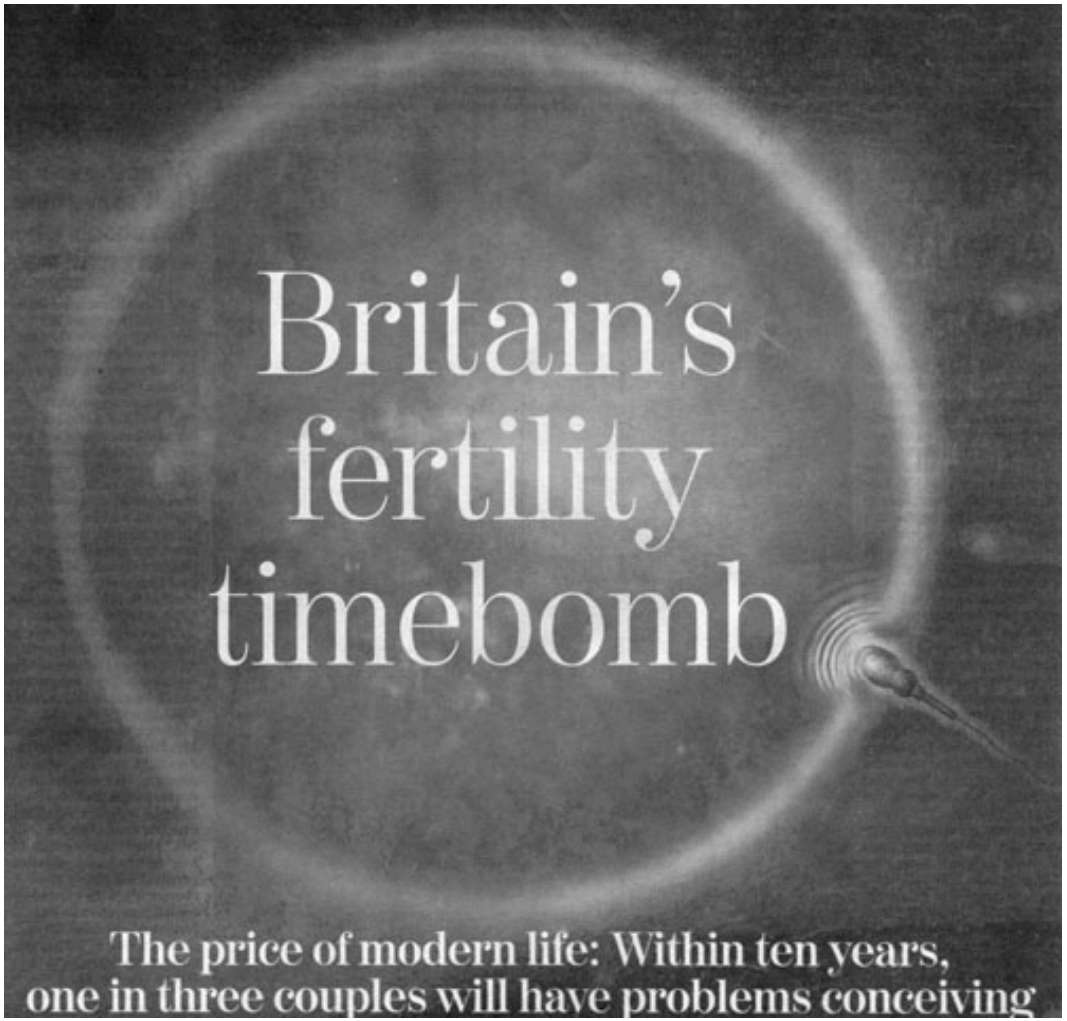
Semen variables and conception in 430 Danish Men



Bonde *et al.*, (1998) The Lancet 352: 1172-1177

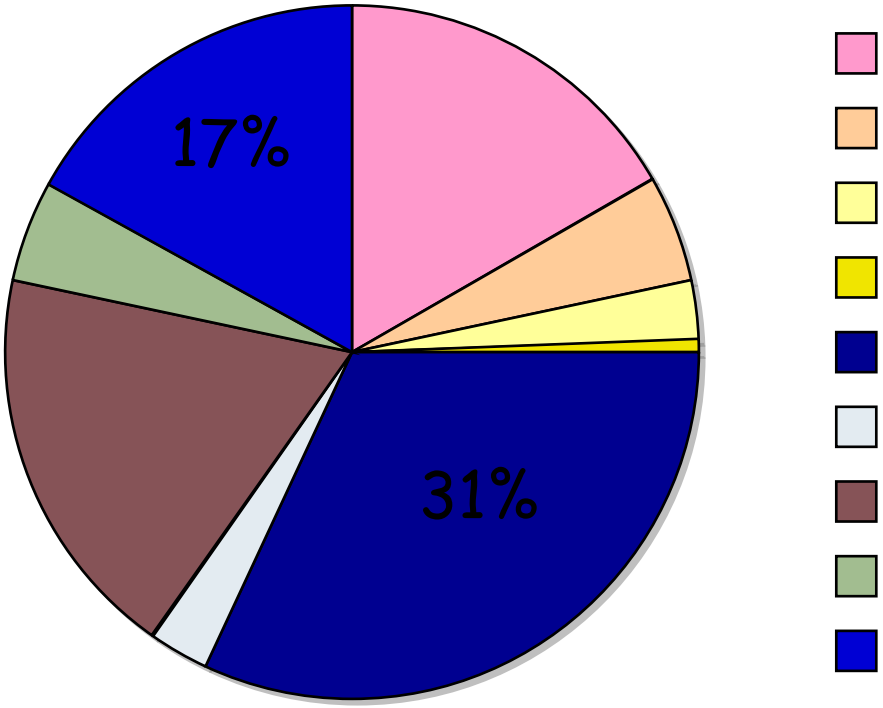
Male Infertility:
the scale of the problem

The changing face of infertility



The Independent 21st June 2005

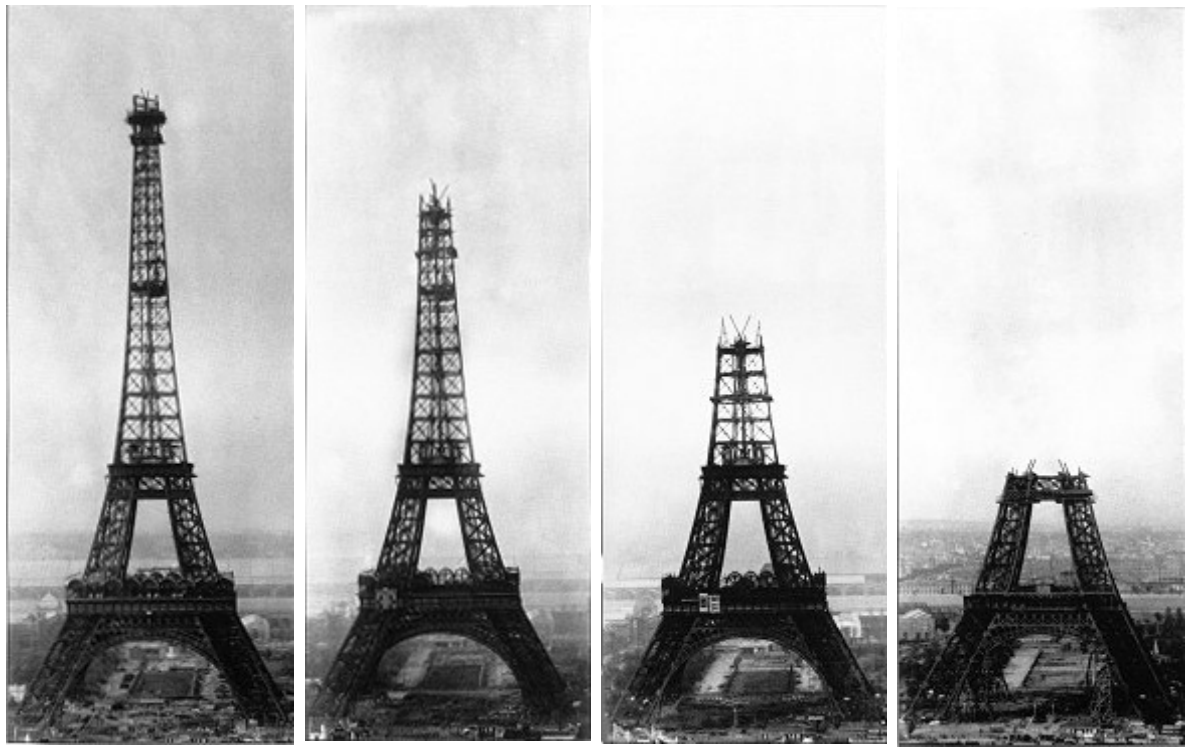
Reasons for infertility



HFEA (2005) The Patient's Guide

Sperm Counts in Parisian men

89×10^6

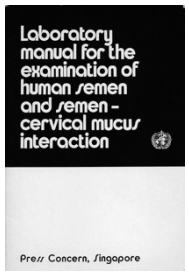
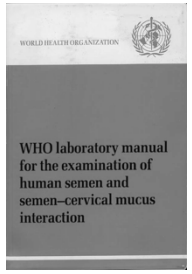
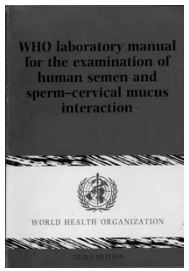
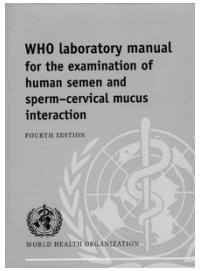


60×10^6

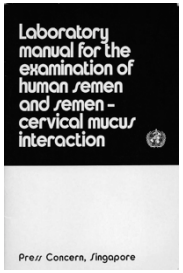
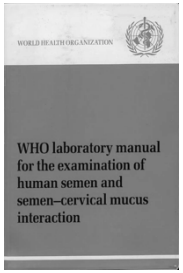
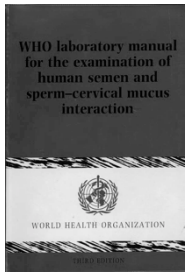
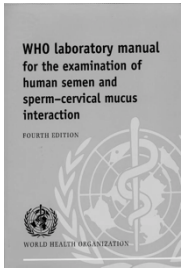
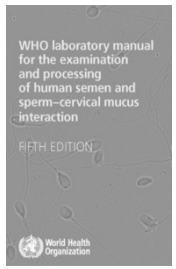
1973 1992

Auger *et al.*, (1992) *NEJM* **332**: 281-285

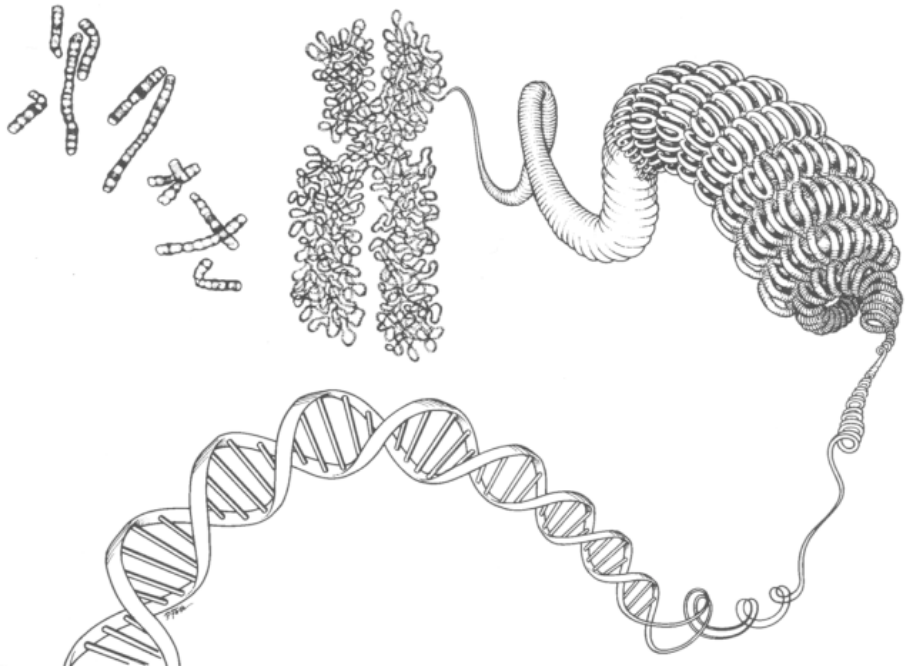
The changing reference ranges

				
Volume	-	≥2.0	≥2.0	≥2.0
Concentration ($x10^6$ ml)	≥20	≥20	≥20	≥20
Motility (% a+b)	≥60	≥50	≥50	≥50
Vitality (% alive)	-	≥50	≥75	≥75
Antibody coated sperm (%)	-	≤10	≤20	≤50

The changing reference ranges

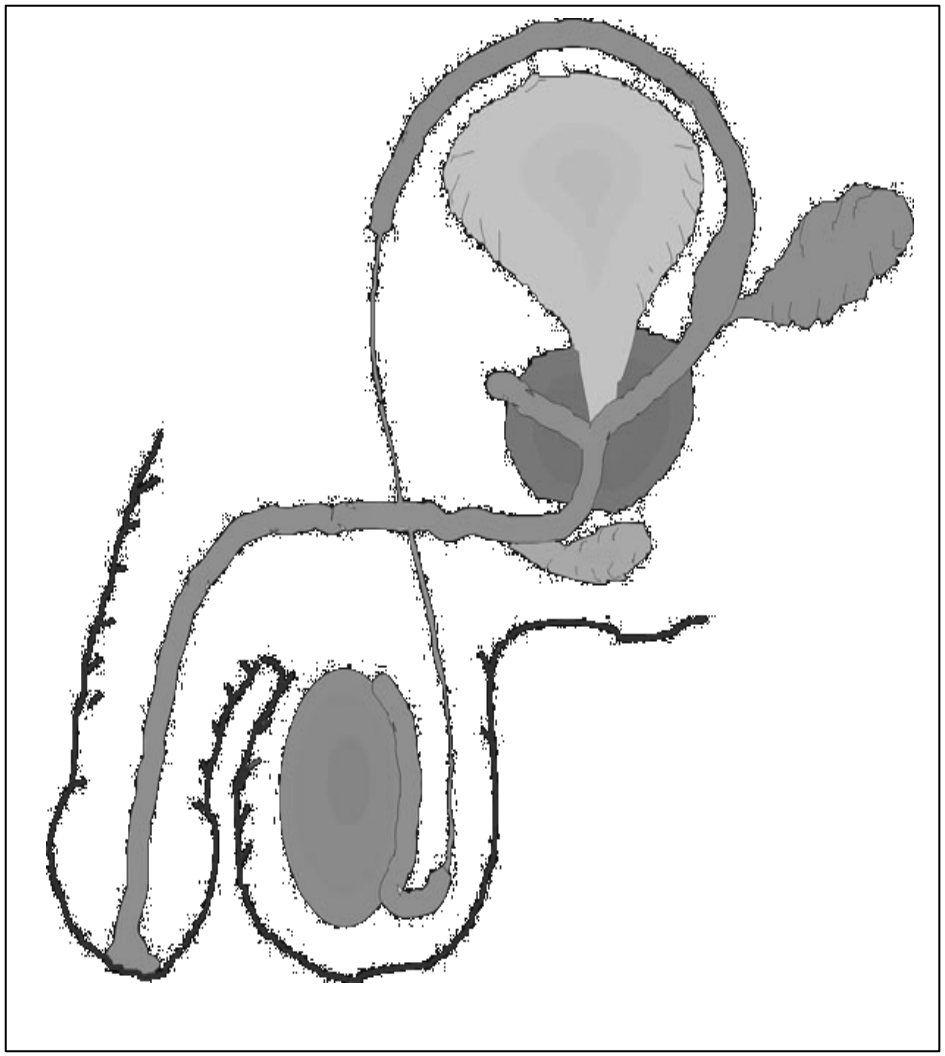
					
Volume	-	≥2.0	≥2.0	≥2.0	≥1.5
Concentration ($x10^6$ ml)	≥20	≥20	≥20	≥20	≥15
Motility (% a+b)	≥60	≥50	≥50	≥50	≥32
Vitality (% alive)	-	≥50	≥75	≥75	≥58
Antibody coated sperm (%)	-	≤10	≤20	≤50	≤50

What can influence poor semen quality?

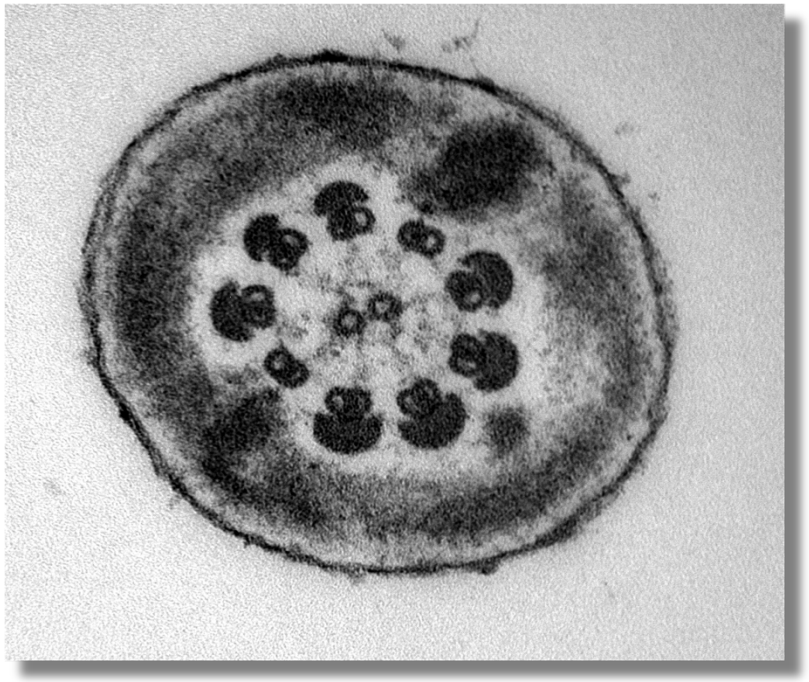


Genetics

Congenital Absence of Vas Deferens



Immotile Cilia Syndrome

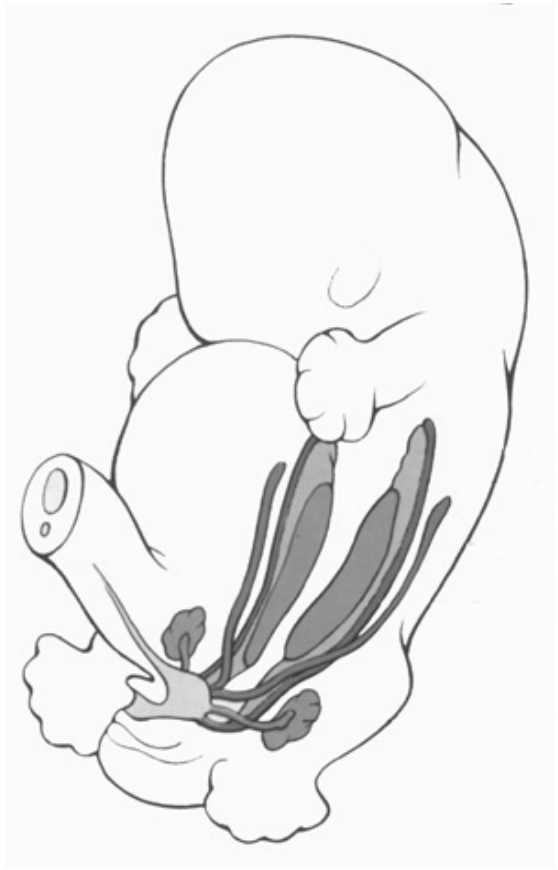


Testicular Development

Testicular dysgenesis syndrome

Environmental factors

Genetic defects or predispositions



Reduced semen quality

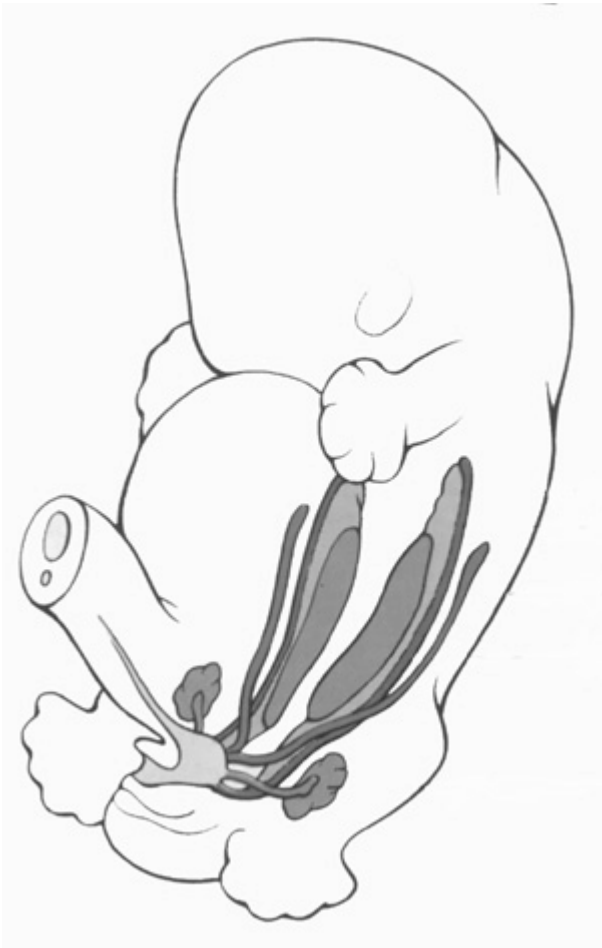
Testicular cancer

Hypospadias

Testicular maldescent

Skakkaebaek *et al.*, 2001 Human Reprod. **16:** 972-978

Smoking in Pregnancy



When mothers smoked > 19 cigarettes per day during pregnancy their sons had:

- 19% lower semen volume
- 17% lower sperm concentration
- 38% lower total sperm count

Compared to unexposed men

Ramlau-Hansen *et al.*, (2007) Am. J. Epidemiol. 165: 1372-9

Beef eating in Pregnancy

Beef link to cut in fertility

MOTHERS who ate large amounts of beef when pregnant are more likely to have sons with weaker fertility, new research suggests.

Women who ate beef every day had sons with a sperm count 24 per cent lower than those born to other mothers, the US study reveals.

Experts believe the damage could have been caused by hormones fed to cattle.

The hormones are now used only by American farmers, being banned in Europe during the 1980s.

The experts want more work done to see whether other chemicals, such as pesticides in food or hormones in water, could be having the same effect.

Sheffield University lecturer Allan Pacey said: "Scientists have been concerned that oestrogen-mimicking chemicals in water supplies, plastics or make-up can affect critical stages in the development of young boys' testicles.

"In extreme cases, this could lead to sperm counts low enough to cause infertility. Europe was justified to ban the hormones."

Some 700 couples were quizzed by Rochester University for the study, published online in the Human Reproduction journal.

FAST-TRACK ARTICLE

Semen quality of fertile US males in relation to their mothers' beef consumption during pregnancy

S.H.Swan[1,4], F.Liu[1], J.W.Overstreet[2], C.Brazil[2] and N.E.Skakkebaek[3]

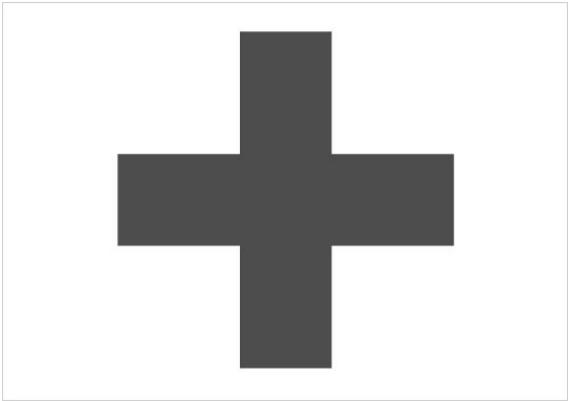
[1]Department of Obstetrics and Gynecology, School of Medicine and Dentistry, University of Rochester, 601 Elmwood Avenue, Rochester, NY 14624, USA; [2]ITEH, University of California, Davis, CA 95616, USA; [3]University Department of Growth and Reproduction, Rigshospitalet, GR-5064, Blegdemsvej 9-2100, Copenhagen, Denmark

[4]Correspondence address. Department of Obstetrics and Gynecology, University of Rochester, School of Medicine and Dentistry, 601 Elmwood Avenue, Rochester, NY 14624, USA. E-mail: Shanna_swan@urmc.rochester.edu.

BACKGROUND: To look at possible long-term risks from anabolic steroids and other xenobiotics in beef, we examined mens' semen quality in relation to their mother's self-reported beef consumption during pregnancy. METHODS: The study was carried out in five US cities between 1999 and 2005. We used regression analyses to examine semen parameters in 387 partners of pregnant women in relation to the amount of beef their mothers reported eating while pregnant. Mothers' beef consumption was also analysed in relation to the son's history of previous subfertility. RESULTS: Sperm concentration was inversely related to mothers' beef meals per week ($P = 0.041$). In sons of 'high beef consumers' (>7 beef meals/week), sperm concentration was 24.3% lower ($P = 0.014$) and the proportion of men with sperm concentration below 20×10^6/ml was three times higher (17.7 versus 5.7%, $P = 0.002$) than in men whose mothers ate less beef. A history of previous subfertility was also more frequent among sons of 'high beef consumers' ($P = 0.015$). Sperm concentration was not significantly related to mother's consumption of other meat or to the man's consumption of any meat. CONCLUSIONS: These data suggest that maternal beef consumption, and possibly xenobiotics in beef, may alter a man's testicular development *in utero* and adversely affect his reproductive capacity.

Keywords: beef; fertility; meat; semen quality; sperm

Swan *et al.*, (2007) Human Reproduction 22: 1497 - 1502



Illness and Infection

Cancer Treatment

Chlamydia and semen quality
(using quantitative PCR)

	Negative (n=87)	Positive (n=13)	
Age (years)	34.69 ± 0.72	33.00 ± 1.82	P = 0.4019
Semen volume (ml)	3.54 ± 0.21	4.66 ± 0.41	P = 0.0287
pH	8.06 ± 0.03	8.16 ± 0.06	P = 0.1749
Sperm concentration ($x10^6$/ml)	70.66 ± 6.08	29.86 ± 6.49	P = 0.0085
Percent motile sperm	45.60 ± 1.17	37.53 ± 4.82	P = 0.0237
Percent of normal morphological forms	10.07 ± 0.42	10.10 ± 1.14	P = 0.0681

Al-Mously *et al.*, (2009) Fertility and Sterility 92: 1606-1615

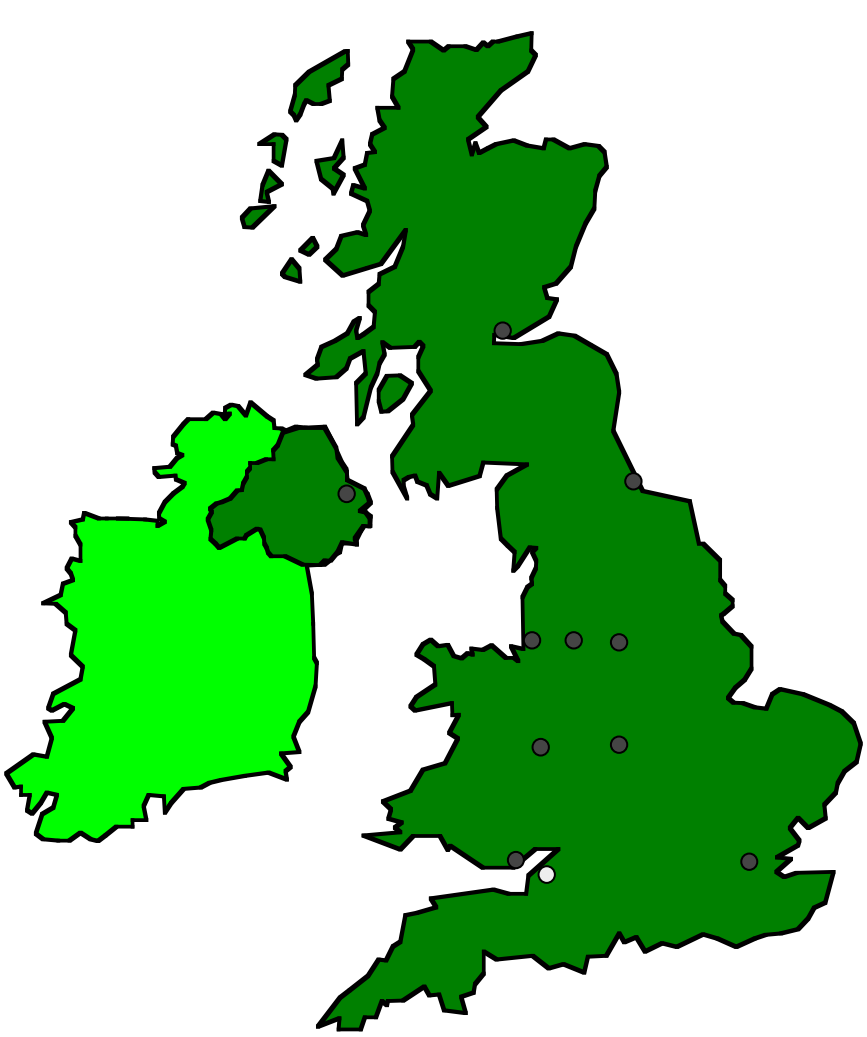
Environment
or
Occupation

Occupation

- 1,230 men in Canada 1972 to 1987 with likely exposure to solvents assessed from occupational questionnaires
- Men with repeated exposure to solvents may be twice as likely to have low motile sperm counts (OR 2.07; 95% CI 1.24 - 3.44)
- In men with high exposure this may be three times more likely (OR 3.83 95% CI 1.37 - 10.65)
- Highest risk occupations include painters, decorators, dry-cleaners, printers and builders.

Cherry *et al.*, (2001) *Occup. Environ. Med.* **58**: 635 - 640

Occupation - CHAPS UK

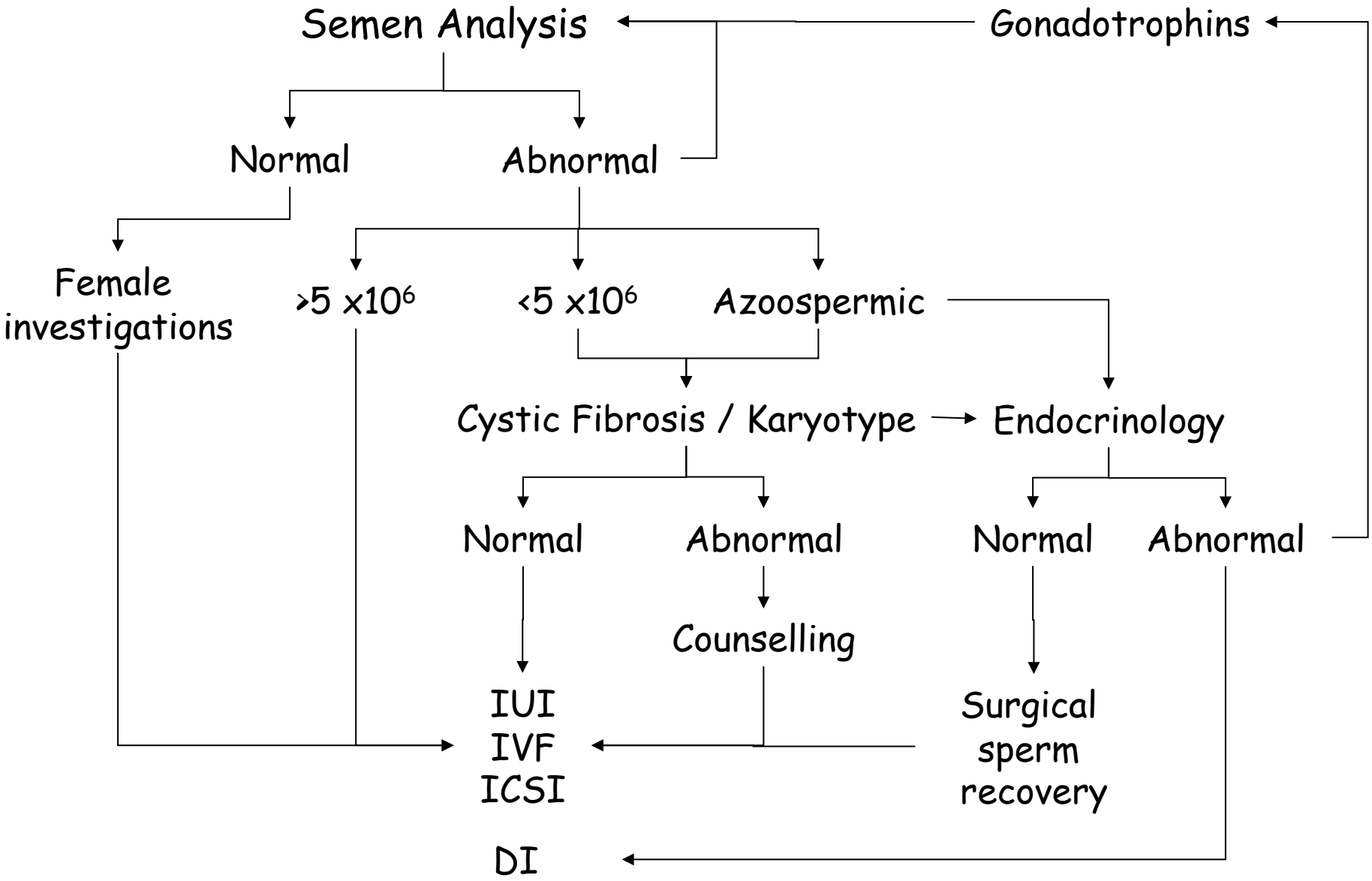


- 2,118 men from 14 UK fertility clinics (1999 to 2002).
- Likely exposure to solvents assessed from occupational questionnaires
- Work with organic solvents in 3 months prior to semen analysis, associated with low motile sperm counts (OR 1.70; 95% CI 1.11 - 2.61)
- No other occupational risk factor was identified.
- No influence of smoking, but wearing of tight underwear was a risk factor.

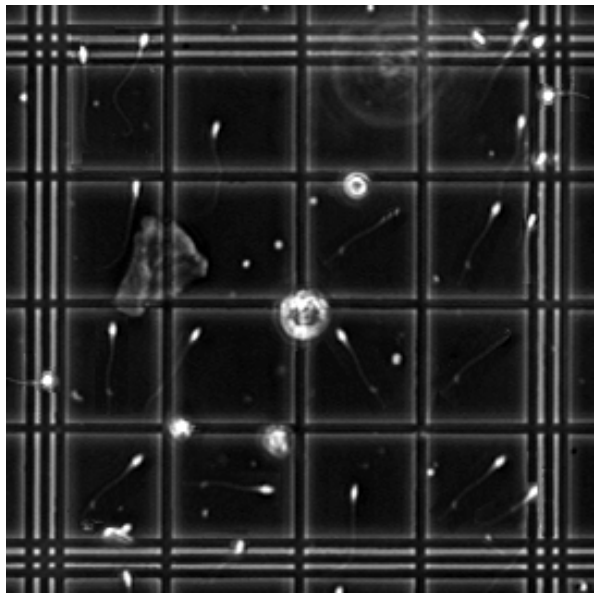
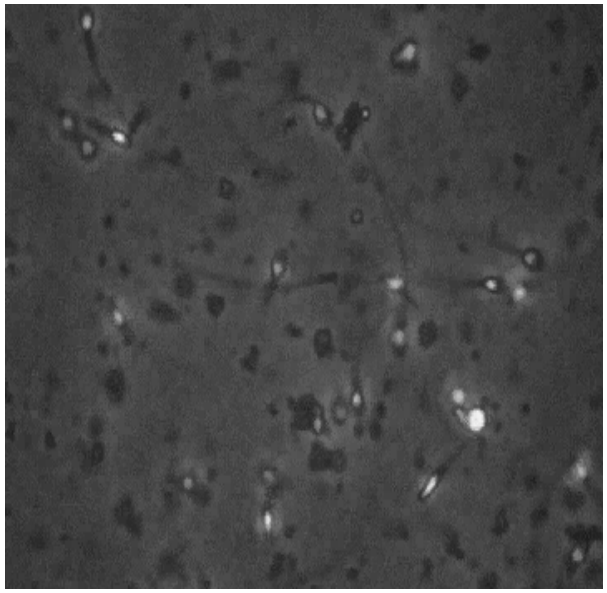
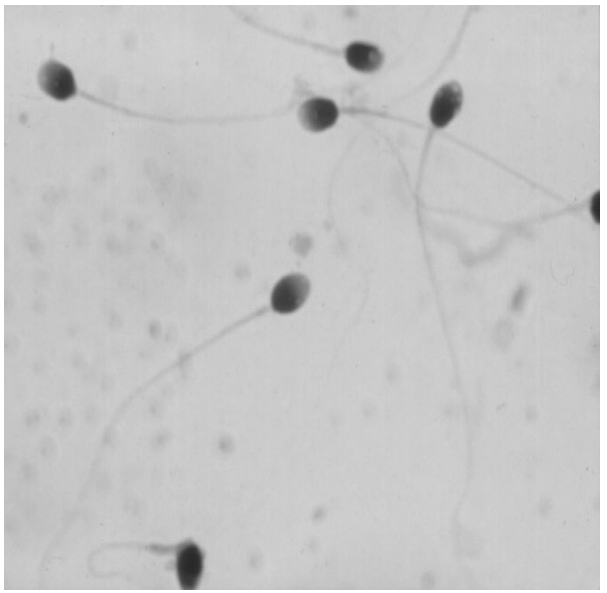
Cherry *et al.*, (2008) *Occup. Environ. Med.* **65:** 708-714

How do we assess male fertility?

Organisation of tests

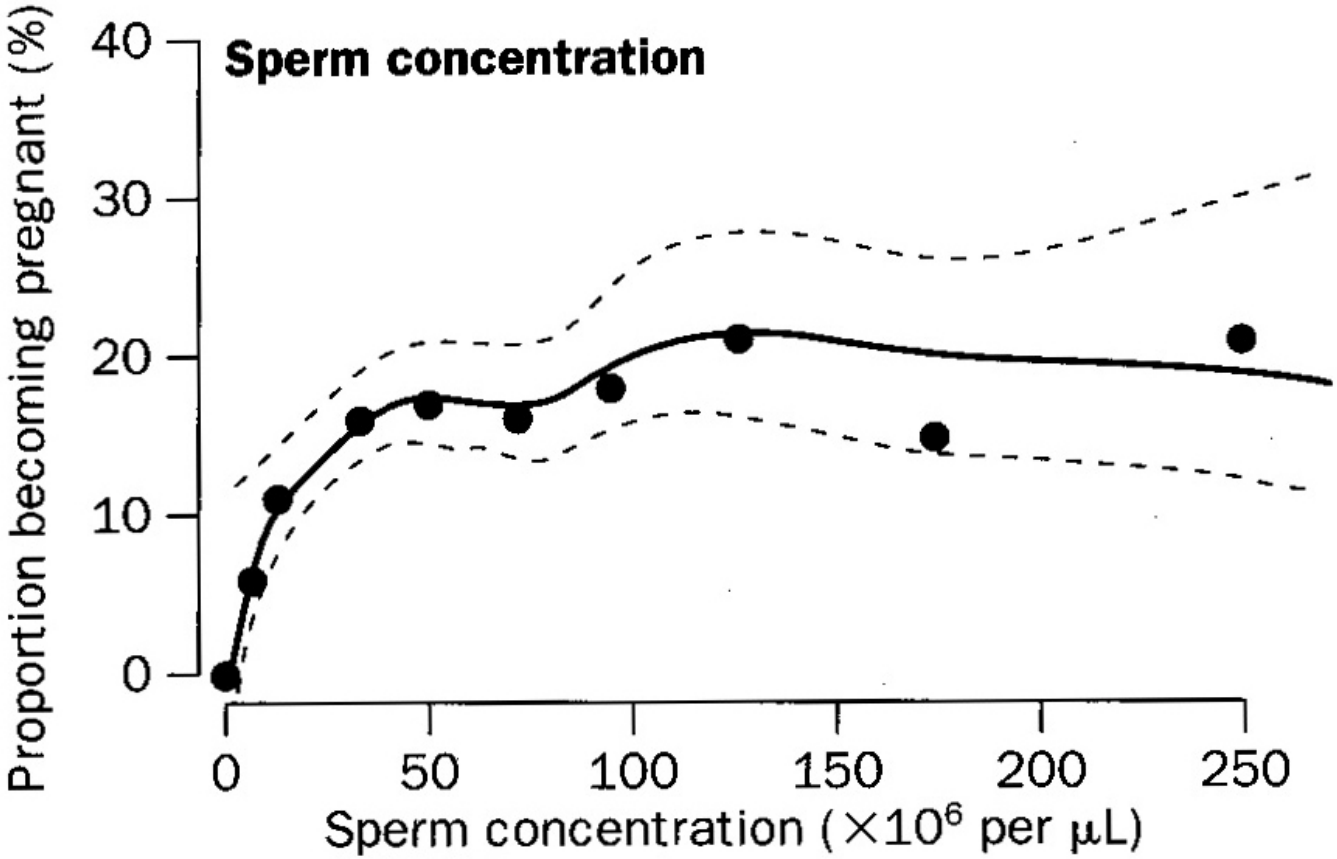


Measures of semen quality

Concentration	Motility	Morphology
		
>15 x 10^6 per ml	>32% motile	>4% 'normal' forms

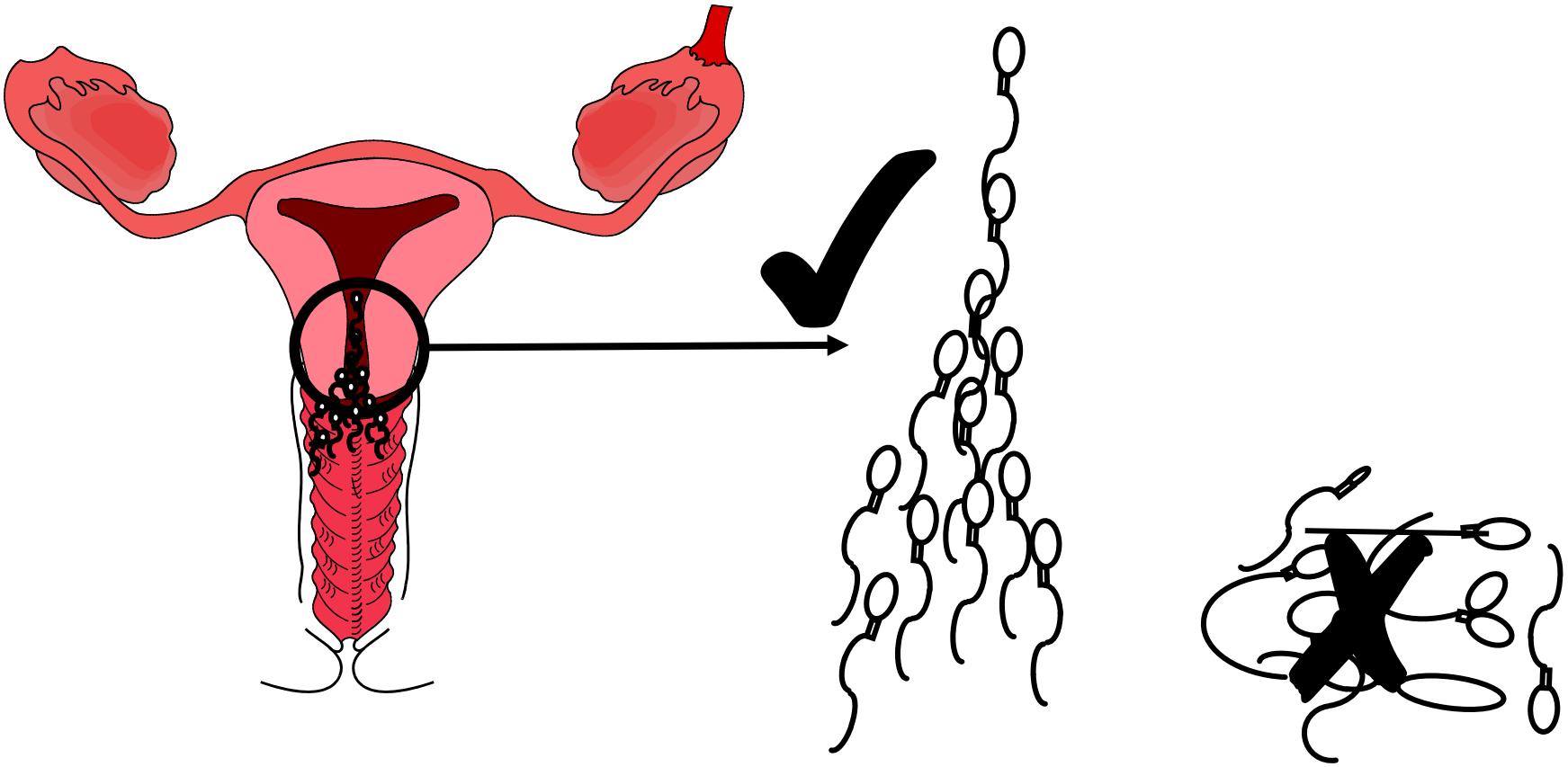
WHO (2010)

Semen variables and conception in 430 Danish Men



Bonde *et al.*, (1998) The Lancet 352: 1172-1177

Sperm Transport



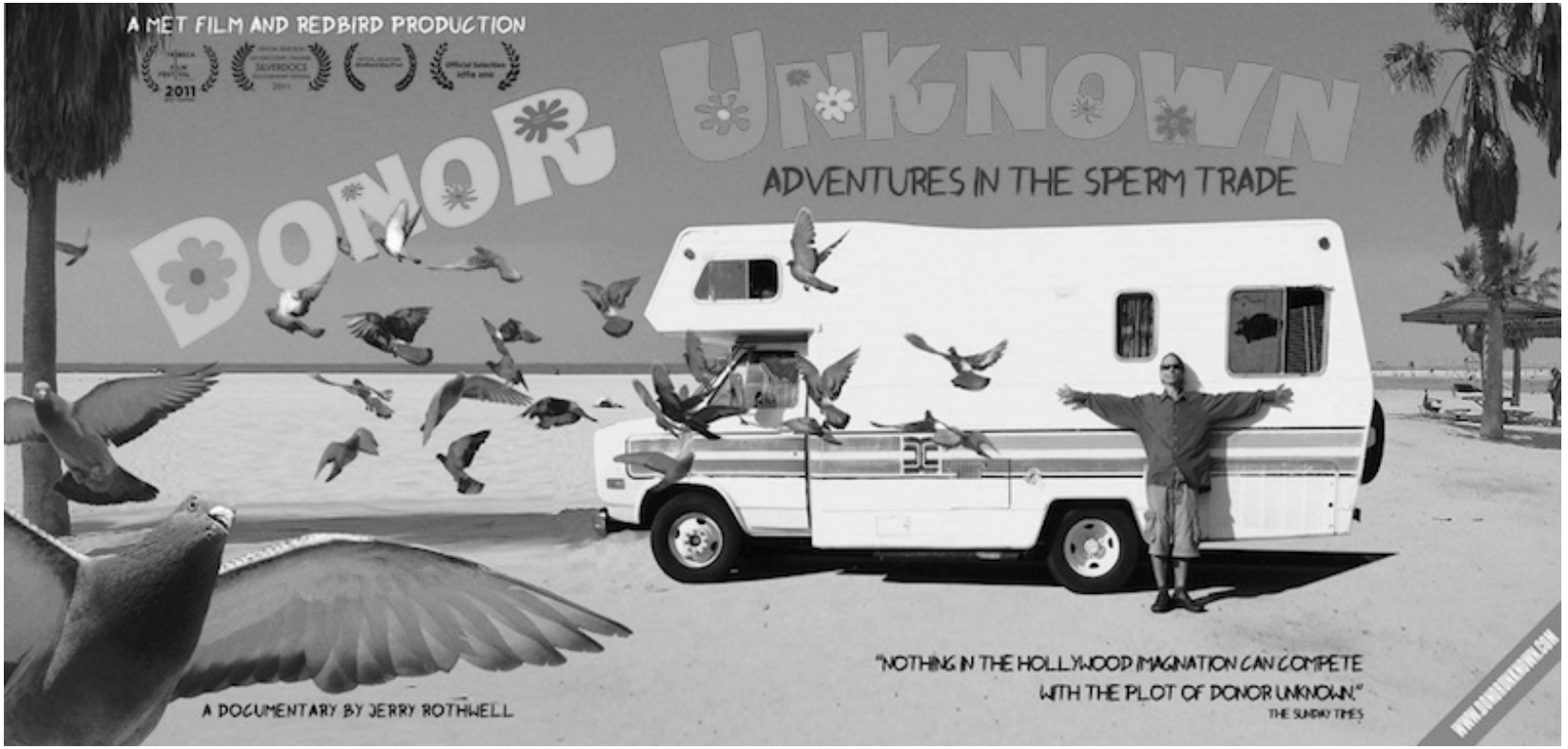
Aitken *et al.*, (1985) J. Reprod. Fertil., 73: 441-449
Katz *et al.*, (1990) Fertility & Sterility 54: 513-516

The Great Sperm Race

Suarez and Pacey (2006) Human Reprod Update 12: 23-37

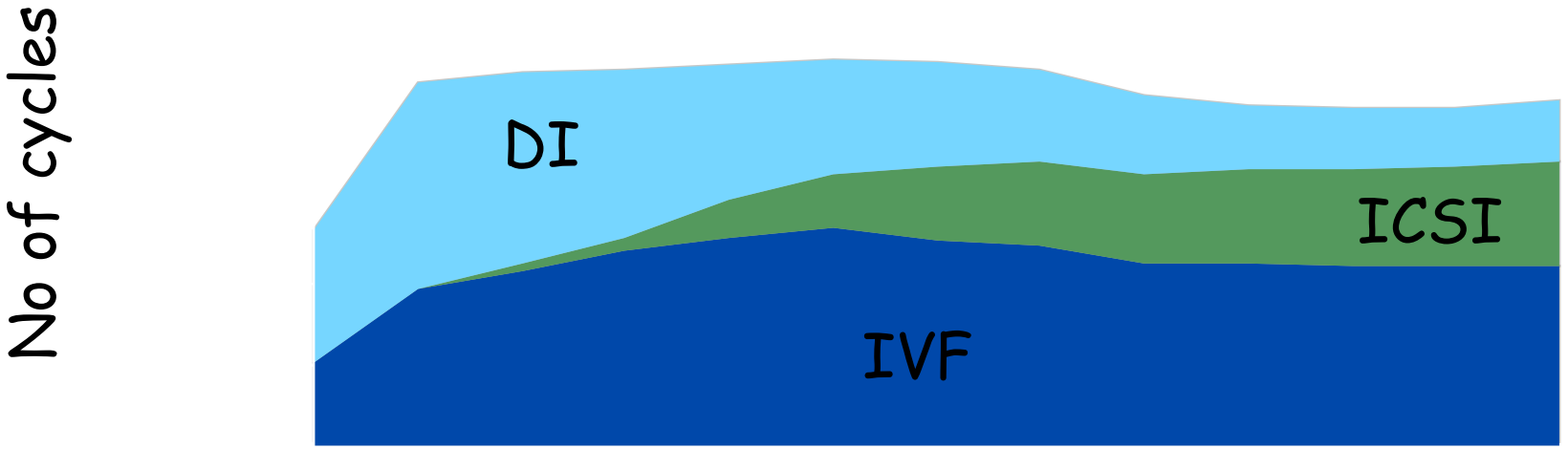
Techniques of Assisted Conception

Sperm Donation



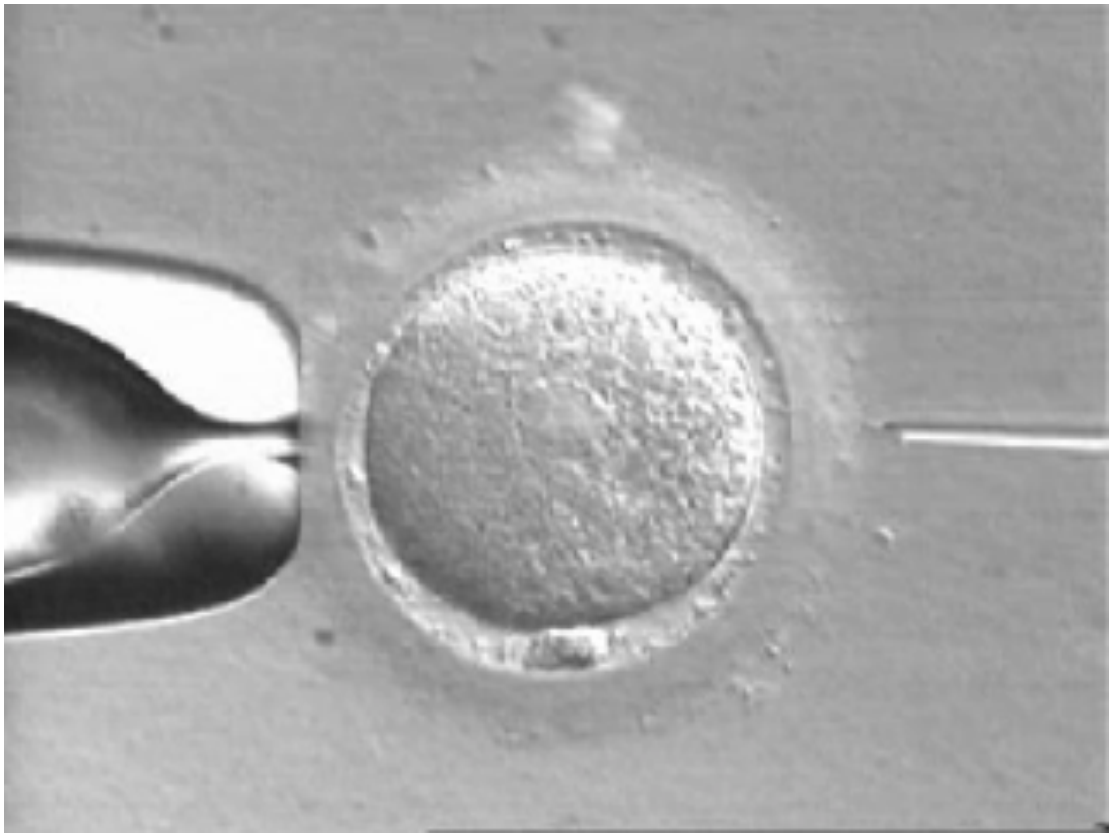
www.donorunknown.com

UK ART Cycles 1991-2004



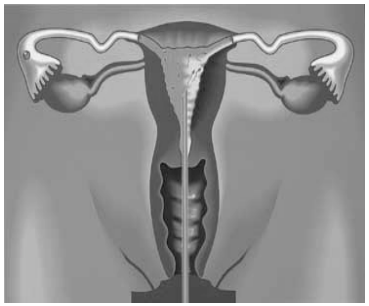
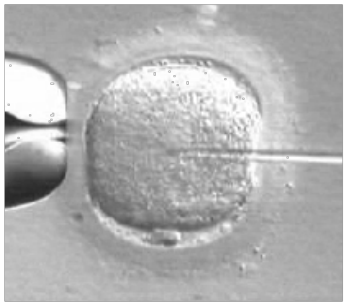
http://www.hfea.gov.uk

Intra Cytoplasmic Sperm Injection



Palermo *et al.*, (1992) *Lancet* **340:** 17-18

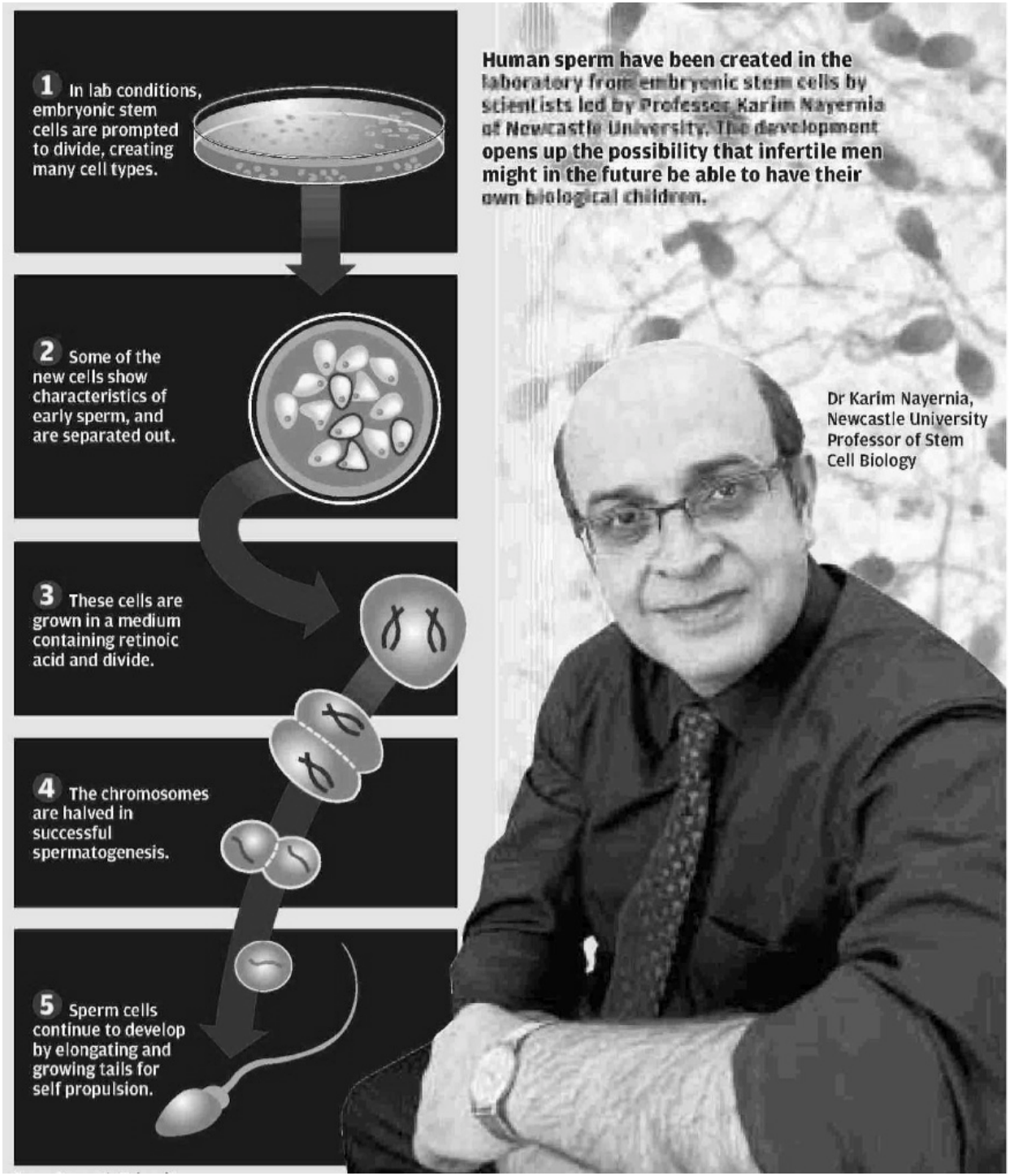
Conception and semen quality

Timed intercourse	IUI	IVF	ICSI	Donor Sperm
				
>15 x 10^6 sperm/ml >32% motile	>5 x 10^6 motile sperm	>1 x 10^6 motile sperm	1 to 1 x 10^6 sperm	azoospermia

European Data in 2003

No of cycles:	79,515	118,919	153,134	15,039
Pregnancy rate:	12.2%	26.1%	26.5%	16.7%

Nyboe Andersen *et al.*, (2007) *Human Reproduction* **22:** 1513-1525



Future developments ?

Summary

- Sub-fertility affects 1 in 6 of the adult population in the UK and in 50% of cases there is a male problem.
- Many factors affect semen quality with pre-natal factors being very important.
- Semen analysis is the main diagnostic tool.
- ICSI has reduced the need for donor sperm treatments but is not suitable for everyone.
- We can't make sperm in the lab – yet!

The University Of Sheffield.

Thank You!

A.Pacey@Sheffield.ac.uk
http://www.twitter.com/allanpacey