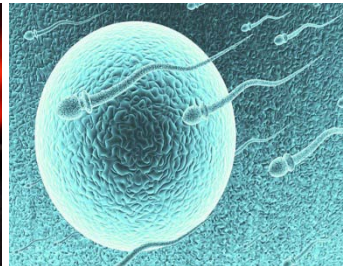


# Recent Advances in Reproductive Medicine

**SUE OPIE**

**RN, BNg Dip M**

**August 2011**





# Learning Objectives

- Understand and identify lifestyle and age factors that affect fertility
- Gain a greater understanding of a Patients perspective having Fertility Investigations and Treatment and Fertility Options available to them
- Understand recent advances/ pregnancy rates in Reproductive Medicine



# Repromed-Dulwich





# REPROMED ART CLINICIANS - AUSTRALIA

*(Listed left to right in alphabetical order)*

## ADELAIDE



Dr Chris Barry



Dr Lisa Bedson



Dr Tricia Davies



Dr Jane Elliott  
(Donor Program)



Dr Simona Fischer



Dr Richard Henshaw  
(Medical Director)



Dr James Harvey



Dr Christine Kirby  
(Clinical Director)



Dr Stephen Lane



Dr Sarah Matthews



Dr Angela McLean



Dr Bruno Radesic



Dr Kelton Tremellen  
(Deputy Medical Director)



Dr Mojgan Vatani



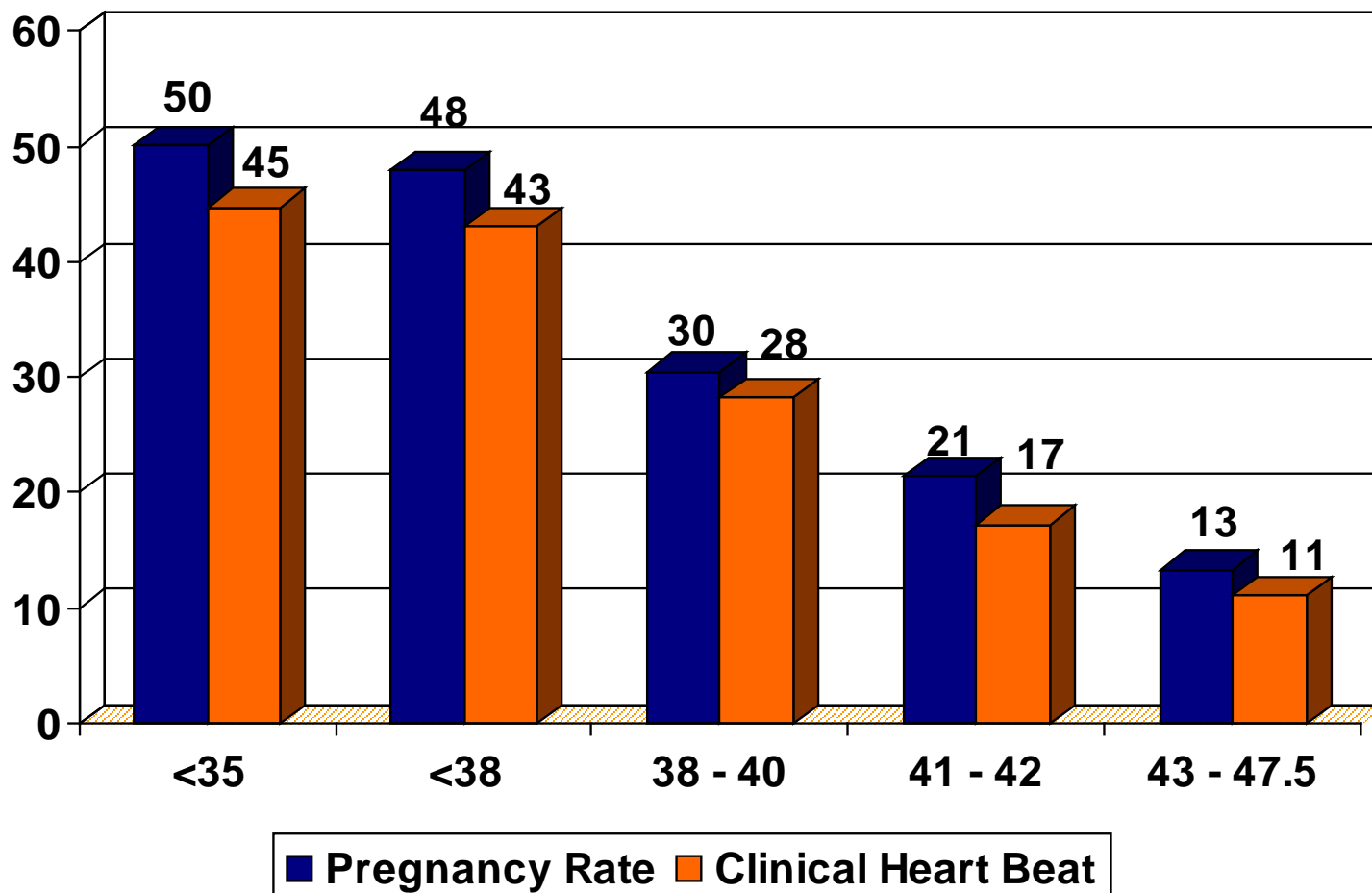
Dr Catherine Videon



Dr Hilary Whittle

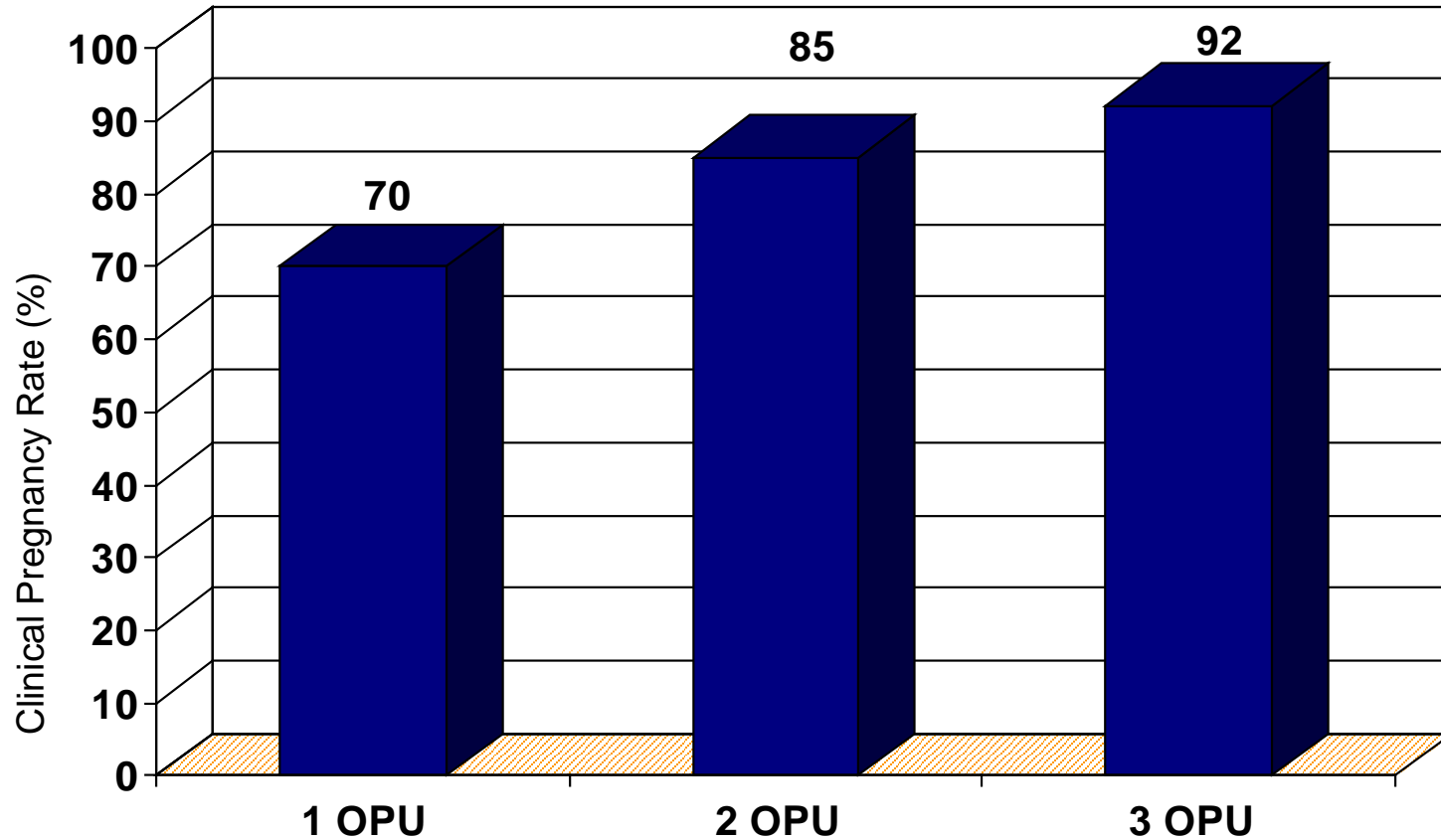


## Jan – Dec 2010 Pregnancy Rates % per Cycle





# Cumulative (Fresh + Frozen Embryo Transfer) Clinical Pregnancy Rates Jan – Dec 2010 - <38 years



(n=2146)



# General Principles

- Infertility Definition:
  - Inability to conceive after 12/12 unprotected intercourse.
- Risk
  - 1:6 couples experience infertility
- Spontaneous conception rates
  - 85% couples conceive after 12/12 trying
  - 95% couples conceive after 24/12 trying
- Causes of Infertility
  - 30% male factor alone
  - 30% female factor alone
  - 30 % dual causation
  - 10 % unexplained infertility
- Lifestyle can impair male and female fertility.



# Preliminary Investigations: Fertility Assessment

## Female:

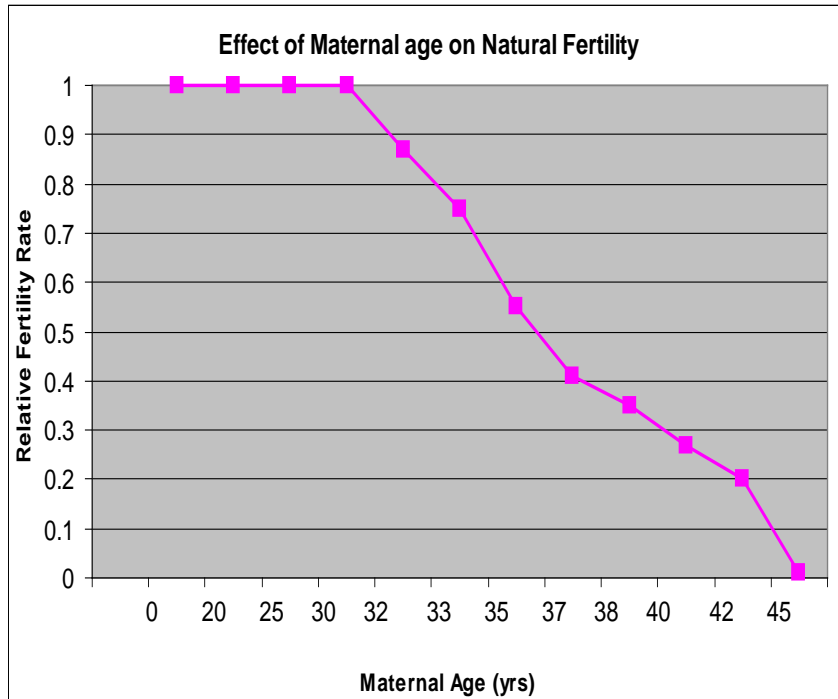
- **Egg Timer Test**
  - Estimates Ovarian Reserve.
  - Single blood test (AMH) and pelvic ultrasound scan
  - Between 3 to 5 days of menstrual cycle or 6<sup>th</sup> to 7<sup>th</sup> day of sugar pill cycle
- Luteal phase progesterone (optional)
- HSG or laparoscopy (unless obvious male factor)
- Lifestyle

## Male:

- Semen-analysis; sperm concn, motility, morphology
  - If abnormal-> FSH, LH, androgen studies, +/- testicular USS, karyotype, Y chromosome microdeletion studies
- Lifestyle



# Female Age and Fertility: Natural Conception



## The “Hutterite Experiment”

Age	Infertile
Under 25	3.5%
25-29	7 %
<b>30-34</b>	<b>11 %</b>
35-39	33%
40-44	87 %
> 45	100 %

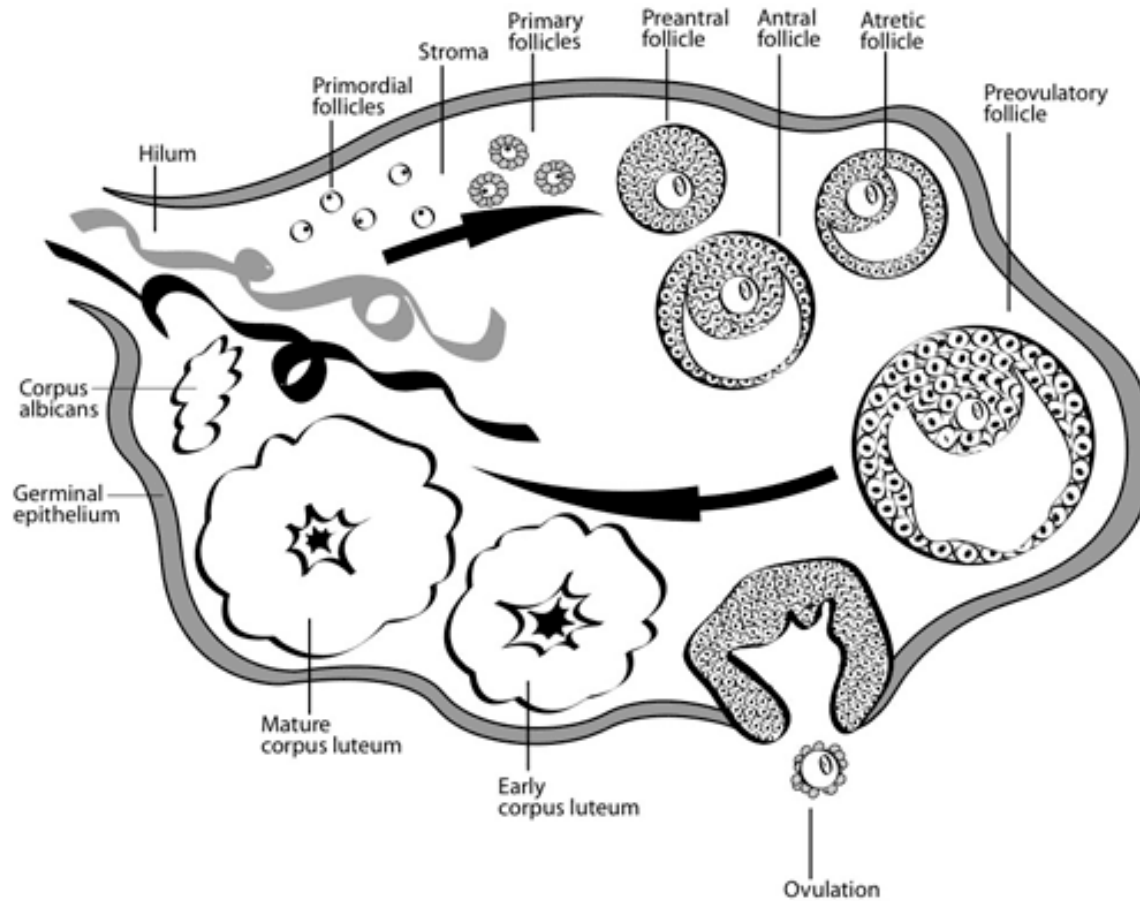
*n = 209 couples*



# Ovarian Reserve Testing

- **Ovarian Reserve** is the term used to describe the number of good quality oocytes (primordial follicles) left within the ovaries.
- **AMH** or anti-mullerian hormone is a good indicator of ovarian reserve.
- Other (less sensitive) indicators of ovarian reserve include **FSH** and **Antral follicle count** on pelvic USS but these measurements are associated with greater observer error and intra-cycle variability.

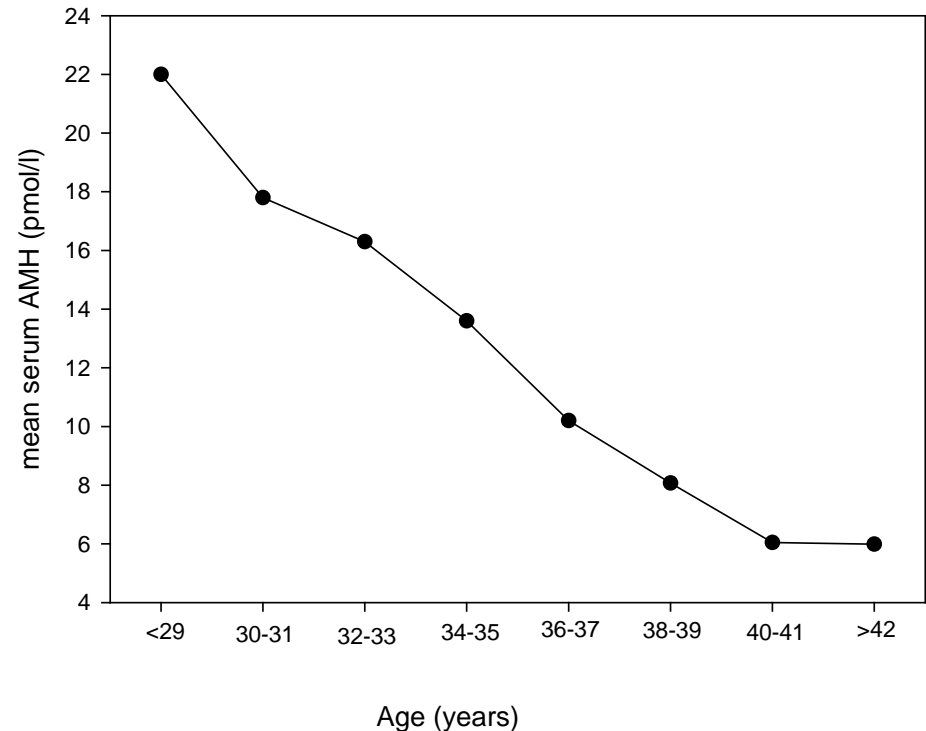
# Stages of Follicular Development





# Relationship between AMH and age

- Survey of 238 women aged 18-46 years.
- Plasma AMH remained relatively static From 18 to 29 years
- On average there was a 50% decline in AMH between 30 and 37 years of age. Despite this large decline in AMH levels, minimal changes in FSH were observed.
- *This highlights the increased sensitivity of AMH compared to the traditional D3 FSH assessment*





# Aging and Fertility: The message women don't want to hear

- Much harder to conceive as women get older.
- Much higher incidence of miscarriage over 35 years old.
- Higher incidence of chromosomal abnormalities as women age.
- Higher incidence of pregnancy complications with advanced maternal age.
- Women may still continue to have periods for up to 10 years after their natural fertility has effectively ended.



# Delaying parenthood

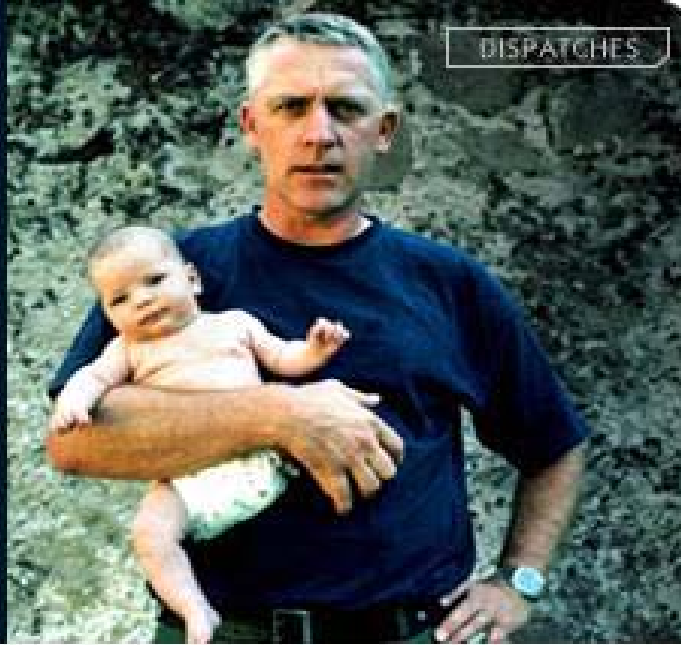
**Old  
New  
Dads**

BY MARK PENN  
AND KINNEY ZALESNE

Why more men are  
having kids in  
their golden years.

photo: Getty

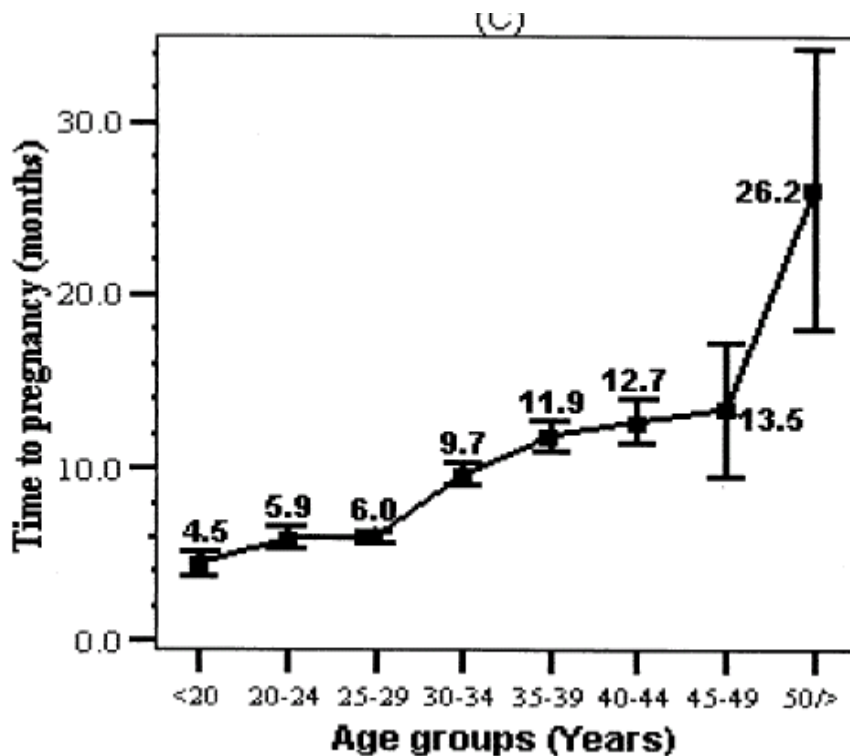
DISPATCHES



Babble.com



# Male age and fertility: Impaired fecundity



- Even when controlling for confounders such as age of the female partner and coital frequency, increasing paternal age has a significant adverse effect on time to conception.
- Men > 45 years of age took 5 times as long to make their young partners pregnant compared to men aged < 25 years.



# Delayed Conception

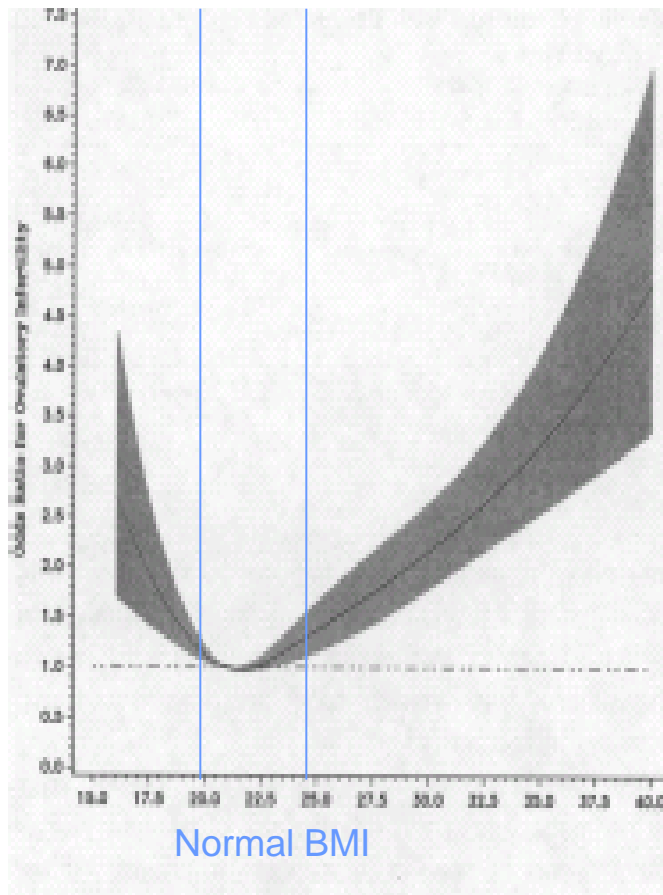
- Complex socio-political issue
- Late marriage
- Inability to find partner
- Career
- Financial stability
- Gross oversimplification to attribute it to women delaying pregnancy



# The Obesity epidemic



# Female BMI and ovulatory disorders



- Nurses Health Study II (Rich-Edwards 2002) examined the relationship between BMI and risk of ovulatory disorders in 116,671 women.
- The risk of impaired ovulation significantly increased if the women was under or over weight.



# “Fitness fanatics” v “lounge lizards”





# Excessive exercise may impair conception

	No Exercise (n=859)	All Categories (n=1,305)	Regular Exercise	
			Category 1 1-3 h/wk for 1-9 y (n=221)	Category 2 4 h or more/wk for 1-9 y (n=230)
Cycle cancellation	1.0 (referent)	1.2 (0.8-1.8)	1.0 (0.5-1.9)	2.8 (1.5-5.3)*
Failed fertilization	1.0 (referent)	1.1 (0.7-1.6)	0.7 (0.4-1.6)	1.2 (0.6-2.6)
Implantation failure	1.0 (referent)	1.3 (1.0-1.6) <sup>†</sup>	1.0 (0.7-1.5)	2.0 (1.4-3.1)*
Pregnancy loss	1.0 (referent)	1.3 (1.0-1.8)	1.3 (0.8-2.2)	2.0 (1.2-3.4)*
Successful live birth	1.0 (referent)	0.8 (0.7-1.0)	0.9 (0.6-1.3)	0.6 (0.4-0.8)*

- A US study tracked exercise levels in 2232 women undergoing their first cycle of IVF and correlated this with treatment outcome.
- 3 or less hours of physical exercise per week did not effect IVF outcomes.
- 4 or more hours of exercise per week resulted in an increase in pregnancy loss and a reduction in live birth rate.
- Moderate exercise is good during IVF to relieve stress but excessive exercise should be avoided.



# Lifestyle #5. Smoking and fertility





# Alcohol and fertility





# Alcohol consumption and fertility

**Table 2** Fecundability odds ratios (95% confidence intervals) according to alcohol intake and sex (logistic regression analysis performed for each sex separately)

Alcohol intake (drinks/ week)	No of cycles	Odds ratio	Adjusted* odds ratio
<b>Women</b>			
0	388	1	1
1-5	771	0.74 (0.54 to 1.01)	0.61 (0.40 to 0.93)
6-10	283	0.73 (0.48 to 1.10)	0.55 (0.36 to 0.85)
11-15	102	0.50 (0.28 to 0.98)	0.34 (0.22 to 0.52)
>15	52	0.66 (0.28 to 1.51)	0.34 (0.11 to 1.07)
<b>Men</b>			
0	151	1.09 (0.68 to 1.76)	0.91 (0.51 to 1.62)
1-5	519	1	1
6-10	390	1.09 (0.77 to 1.54)	1.02 (0.68 to 1.51)
11-15	229	0.76 (0.48 to 1.19)	0.76 (0.46 to 1.26)
>15	307	0.82 (0.55 to 1.23)	0.83 (0.53 to 1.30)

- Danish study of 430 couples aged 20-35 years attempting first conception found a link between alcohol consumption and fecundity.
- Consumption of any alcohol by a woman impaired her fertility.
- The effect of alcohol on male fertility is relatively minimal up to 2 drinks per day.
- Women should be instructed to avoid alcohol when trying to conceive



# STDs and fertility



- 8% of asymptomatic women < 25 years of age attending a NZ FPA clinic were found to have Chlamydia on screening (Sparrow et al 2007).
- The incidence of tubal infertility after 1 episode of PID is 12%, 23% after 2 episodes and 54% after 3 episodes of PID (Westrom et al 1980).
- Use of condoms in new relationships and opportunistic screening of young men and women is vital to reduce the chances of infertility.



# Common Fertility Treatment Options

- **General** eg. Lifestyle, IC timing, weight loss, smoking etc
- **Ovulation Induction** eg clomid, preferably with cycle tracking and timed intercourse
- **Intra-uterine Insemination (IUI).**  
Pregnancy rates 17-20%  
Increased chances multiple pregnancy
- **IVF +/- ICSI**  
Pregnancy rates 50-52%  
Low chances multiple pregnancy if single embryo transfer



# IVF

- **Stimulation** of greater numbers of eggs in the ovaries
- **Collection** of the eggs in day surgery- vaginal USS and pv aspiration of ovarian follicles
- **Sperm sample** produced/collected
- Eggs **fertilised** via standard IVF or microinjection
- **Embryos** grown to day 4-5
- Best **embryo transferred** to uterus
- Remaining suitable **embryos frozen**
- **Pregnancy test** approximately 31 days after starting cycle
- 50-52% pregnancy rates for women under 38 years old

# In Vitro Fertilisation

**Oocyte collection**

(TVOR, Laparoscopy)

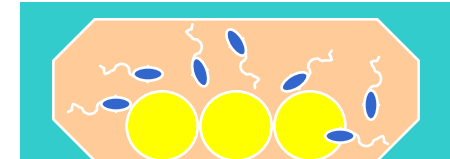
**In vitro maturation**



**Sperm collection**

**Storage & capacitation**

**In vitro fertilisation**



Simple medium  
18 h incubation

**In vitro culture**





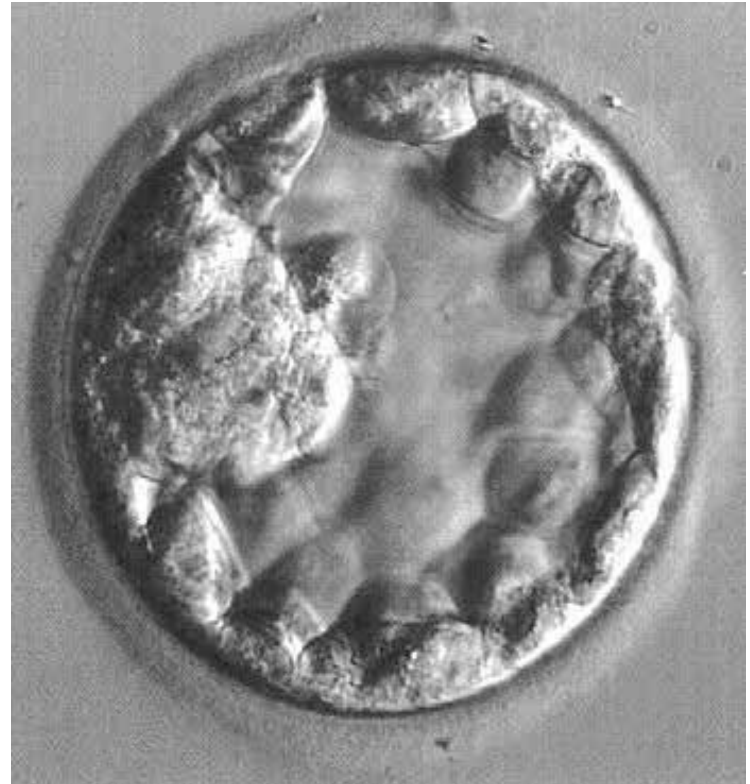
## Recent advances *continued*

Extended culture, metabolomics, vitrification techniques

- Day 3 embryo



- Day 5 blastocyst



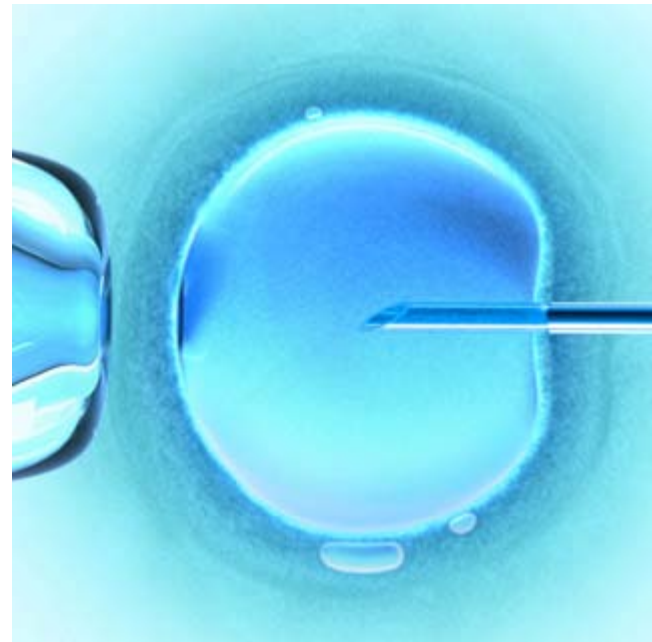


# IVF or ICSI/microinjection

- Standard IVF

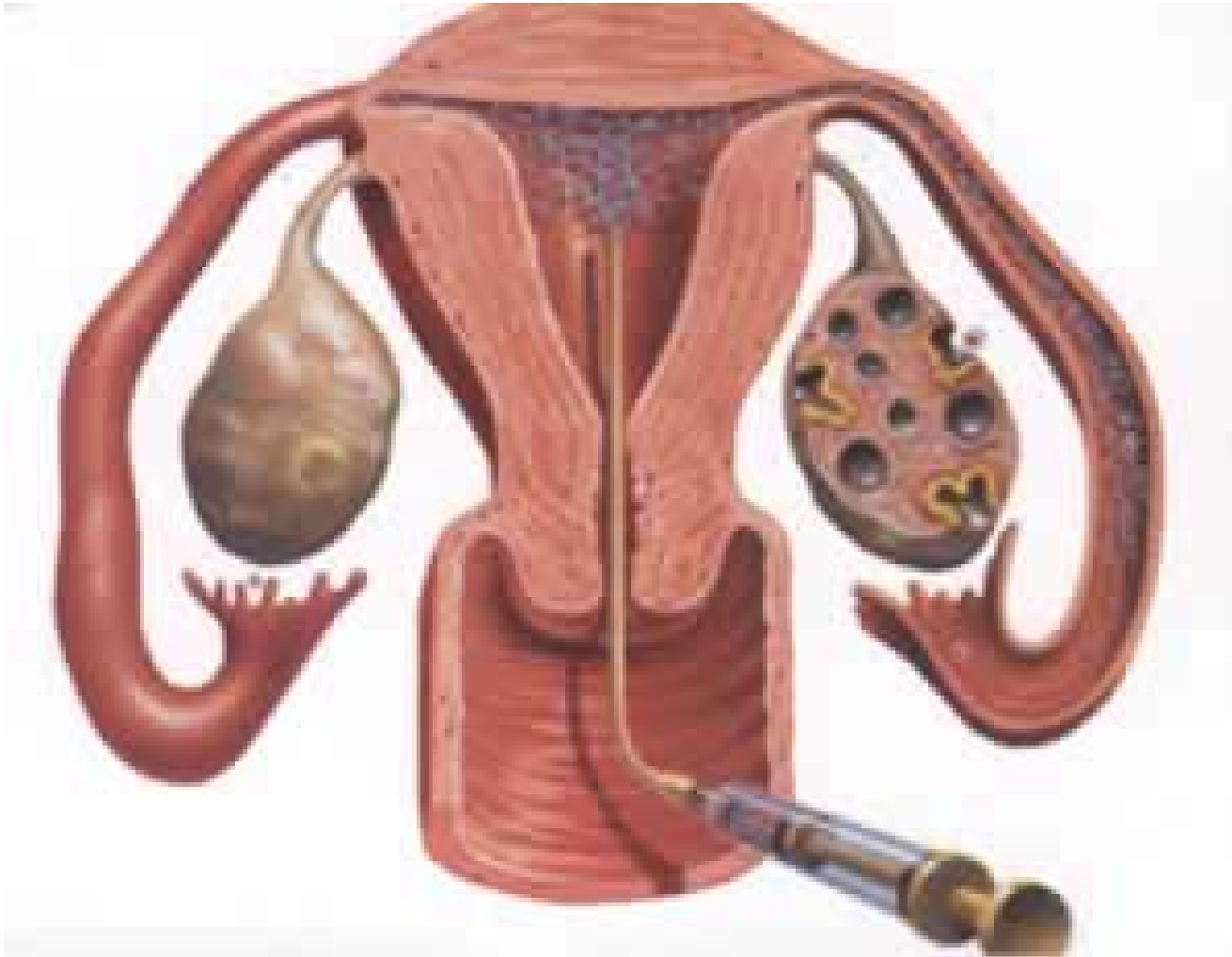


- ICSI/ microinjection





# Intra-Uterine Insemination- IUI





# Ultrasound appearance of polycystic ovaries





# PCOS Treatment Options

- Lifestyle, weight loss, exercise
- Ovulation Induction, metformin, clomid- preferably with cycle tracking and timed intercourse
- Ovarian Drilling
- Intra-Uterine Insemination
- IVF



# Recent Advances in Reproductive Medicine

1. Ovarian Reserve Testing and AMH-delayed parenting
2. Extended Embryo Culture
3. Antagonist cycles- shorter more patient friendly
4. Menevit
5. DNA integrity testing (TUNEL) and TESA sperm
6. Egg freezing and fertility preservation; Pre-cancer treatments, predicted premature ovarian failure, elective/social
7. New embryo freezing techniques- Vitrification
8. New embryo selection techniques- Metabolomics



# Patients Perspective

- VISITS TO REPROMED
  - Doctors appointments
  - Nurse Education Sessions / Drug Collection
  - Blood tests / Ultrasound scans
  - Day Surgery
  - Embryo Transfer
  - Counselling



# Patients Perspective

- Travel
- Telephone Calls, SMS, Email
- Time off work

