



European Society of Human Reproduction & Embryology

**ESHRE Campus 2008
Ovarian reserve – Modena (Italy), April 18-19**

Fertility and reproductive ageing

P.G. Crosignani (Milano)

- A) Measurements of the reproductive function
- B) Spontaneous fertility and ageing
- C) Effect of age on ART

A – Reproductive function and ageing

- In women and men the function declines with age.
- Women abruptly lose fertility at menopause (“to avoid the risks of pregnancy”, Cohen, 2004).
- Male fertility declines slowly and progressively after 35, but some are still fertile after 70.



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A – Measurements of the reproductive function in a general population.

- **FECUNDABILITY**
Is the probability of achieving pregnancy within one menstrual cycle.
- **FECUNDITY**
Is the ability to achieve a live birth from exposure to the risk of pregnancy for one cycle.

(The ESHRE Capri Workshop Group, Human Reproduction, 11, 1775-1807, 1996)



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A – Measurements of the reproductive function in a general population.

- FERTILITY

Based on the distribution of fecundity observed in a "normal" population, normal fertility is defined as achieving a pregnancy within two years by regular coital exposure.

(The ESHRE Capri Workshop Group, Human Reproduction, 11, 1775-1807, 1996)



A – Demographic measures of fertility

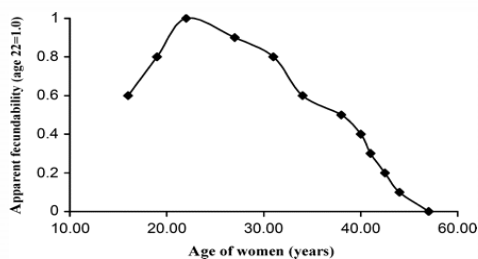
Are based on the woman:

- Only in a strictly monogamous society will reflect couple- infertility.
- Voluntary and involuntary childlessness cannot be distinguished.

(The ESHRE Capri Workshop Group, Human Reproduction, 11, 1775-1807, 1996)



B – Natural fecundability and woman's age (retrospective study)



(Homan et al., HRU, 13, 209-223, 2007)



B – Time to spontaneous pregnancy and woman's age (prospective studies)

| | | |
|----------------------------|-----|-----|
| Age (yrs) | <30 | ≥36 |
| Conception in 3 months (%) | 71 | 41 |

(Kaplan et al., EJOG, 123, 72-76, 2006)

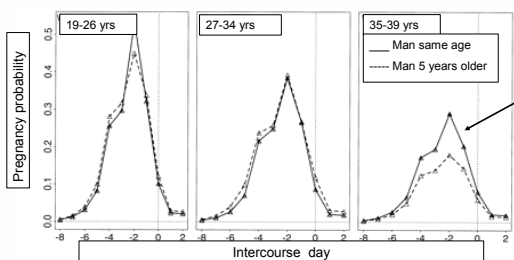
| | | |
|-------------------------------|-----|------|
| Age (yrs) | <25 | ≥ 35 |
| Conception after 2 years (RR) | 1 | 2.2 |

(Hassan and Killik, FS, 81, 384-392, 2004)



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B – Midcycle fecundity in ovulatory cycles and age

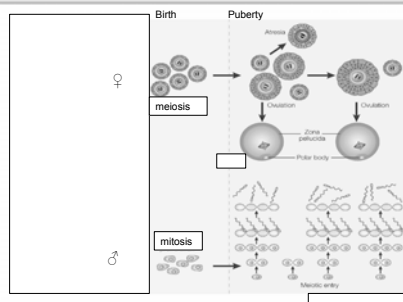


(Dunson et al., HR, 17, 1399-1403, 2002)



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B – Sex-specific differences in the onset and duration of meiotic processes



(The ESHRE Capri Workshop Group, HRU, 11, 261-276, 2005)



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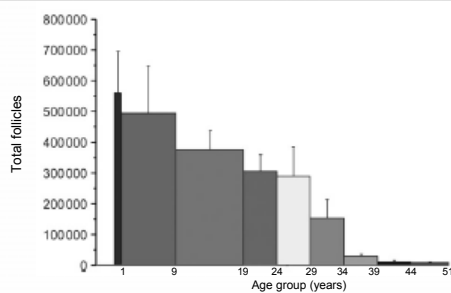
B – The ageing ovary

- Fewer follicles
- Worse oocytes



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B – Follicles decay faster with increasing age



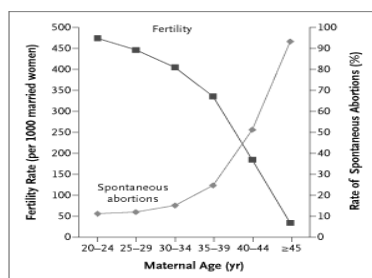
* The height of the bar represents the average NGF count for the given age group \pm SEM. The width of the bars represents the number of years included in the given age group.

(K.R. Hansen et al., H.R., 23, 699-708, 2008)



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B – Worse clinical outcomes linked to oocyte quality

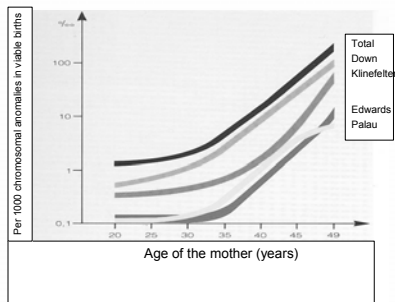


(Heffner, NEJM, 351, 1927-1929, 2004)



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B – Chromosomal abnormalities and woman's age



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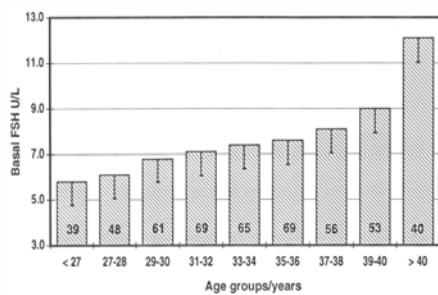
B – Symptoms and indices of ovarian ageing

- Gradual shortening of the menstrual cycle
- FSH \uparrow
- Inhibin B \downarrow
- Anti-Mullerian hormone (AMH) \downarrow
- Total antral follicles \downarrow
- Ovarian volume \downarrow



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B – FSH and ovarian ageing



(Ebbiary et al., 1992)



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B – The ageing male

- The percentages of motile sperm cells and sperm cells with normal morphology slowly decline with age
- Sperm concentration: data are conflicting
- Few studies on sperm cell function

(The ESHRE Capri Workshop Group, HRU, 11, 261-276, 2005)



B – The ageing male

- Impotence became more frequent with age
- Chromosomal anomalies in sperm:
since the initial incidence is very low, the increase observed is not clinically relevant

(The ESHRE Capri Workshop Group, HRU, 11, 261-276, 2005)

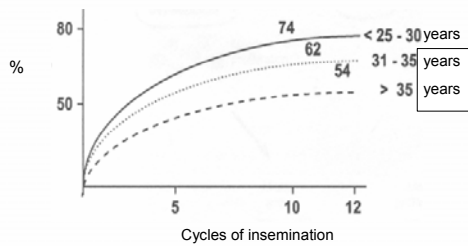


C – The effect of age in couples undergoing ART cycles

- Donor insemination
- IVF - ICSI



C – Donor insemination cycles: cumulative pregnancy rates in relation to age of the women

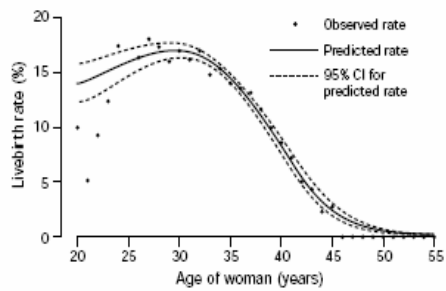


(Federation Cecos, NEJM, 1982)



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C – UK IVF success rates in relation to maternal age



(Templeton et al., Lancet, 348, 1402-1406, 1996)



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C – IVF: age is a better predictor of pregnancy potential than basal FSH

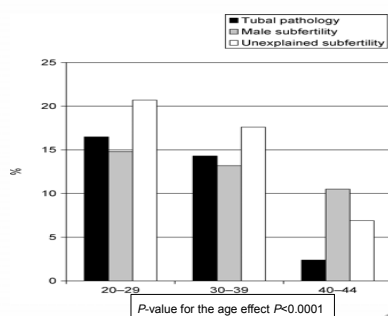
- 1045 women at their first IVF cycle

(C.C. Chuang et al., FS, 79, 63-68, 2003)



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**C – IVF birth rate: the effect of woman's age
(8457 women)**



(Linsten et al., HR, 20, 1867-1875, 2005)



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**C – ICSI: effect of maternal age on success rate
(obstructive azoospermia)**

| Mother's age (years) | No. of cycles | Delivered pregnancies (% per cycle) |
|----------------------|---------------|-------------------------------------|
| <30 | 42 | 50 |
| 30-36 | 68 | 37 |
| 37-39 | 12 | 17 |
| 40+ | 14 | 7 |

(Silber et al., HR, 12, 2693-2700, 1997)



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**C – ICSI effect of father's age
(female partners aged ≤35 years)**

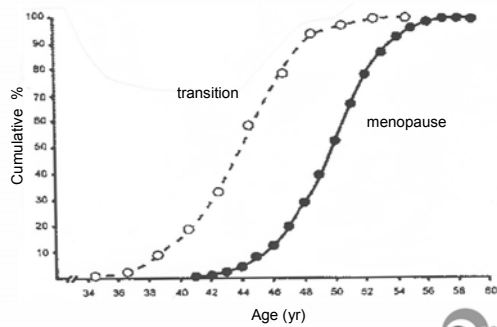
| Age (years) | Males (no.) | Clinical pregnancies/cycle (%) |
|-------------|-------------|--------------------------------|
| ≤35 | 310 | 55 |
| 36-39 | 79 | 42 |

(Spandorfer et al., HR, 12, 334-338, 1998)



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The transition period and human reproduction



(Treloar, Maturitas, 3, 249-264, 1981)



D – Social determinants of human infertility

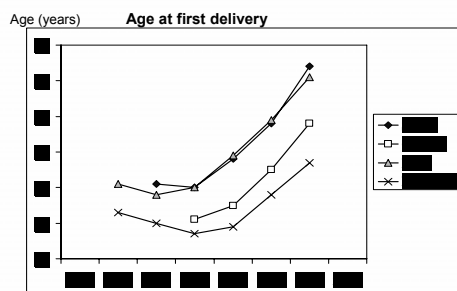
Age at marriage

| Woman's age | Infertility (%) |
|-------------|-----------------|
| 20-24 | 5.7 |
| 25-29 | 9.3 |
| 30-34 | 15.5 |
| 35-39 | 29.6 |
| 40-44 | 63.5 |

(Menken et al., Science, 1986)



D – Social determinants of human infertility



(The ESHRE Capri Workshop Group, HRU, 11, 261-276, 2005)



C – ART make-up for the births lost by postponing conception

| Conception postponed (years of age) | ART make-up |
|--|-------------|
| From 30 to 35 | 50% |
| From 35 to 40 | 30% |

(The ESHRE Capri Workshop Group, HRU, 11, 261-276, 2005)





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D – Social determinants of human infertility Conception is sistematically postponed

Most educated women overestimate the chances of achieving pregnancy after 35

(Lampic et al., HR, 21, 558-564, 2006)



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Conclusion

- Social factors are the main determinants of human reproduction
- In many European Countries the woman's age is the first cause of infertility
- ART can only help a proportion of these couples
