Fertility, infertility and the use of Assisted Reproductive Technology (ART) – a European Perspective

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Human reproduction

Reproductive situation

• The voluntary fertile
• The voluntary infertile
• The involuntary fertile
• The involuntary infertile

Medical care

The deliveries (100 years)
Contraception (50 years)
Legal abortions (40 years)
Infertility (30 years)

These 4 aspects of human reproduction should be considered as a whole – European societies offer citizen’s assistance regarding all 4 aspects of their reproductive life – also for couples with infertility…….
Infertility –
Not a new problem – but new treatments

In “marriages which had lasted five years or more, and in which the husbands were under 75 years of age, ... one marriage in 6·5 was unproductive".

J Y Simpson
Survey of 495 British Peers, cited in Gibbons (1911)
“Assisted reproductive technology”

*Finally* full recognition - *The Nobelprice...*
Part I. The fertility in Europe

Demographers use the ”Total Fertility Rate” TFR defined as the number of children born per woman during her reproductive live-span – to measure the fertility in the population.

In order to have a stable population each woman should have 2.1 children (replacement levels)
Total fertility rates (TFR) in Europe

Number of children per woman
Fertility. A demographic challenge

Total fertility rate below “replacement levels”
Demographic change towards an elderly population

Portugal
Stable and much below the replacement level of 2.1

2000 1.47 children / woman
2003 1.49 children / woman
2004 1.46 children / woman
2005 1.47 children / woman
2008 1.49 children / woman

TFR’s below 1.5 have been named ”the fertility trap”…because it takes generations to restore the fertility
### Fertility desires in Europe

<table>
<thead>
<tr>
<th>Countries</th>
<th>Average desired number of children (women)</th>
<th>Average desired number of children (men)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Austria</td>
<td>1.84</td>
<td>1.78</td>
</tr>
<tr>
<td>Belgium</td>
<td>1.86</td>
<td>1.81</td>
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<tr>
<td>CZ Republic</td>
<td>1.97</td>
<td>2.02</td>
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<td>Estonia</td>
<td>2.16</td>
<td>2.09</td>
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<tr>
<td>Finland</td>
<td>2.18</td>
<td>2.14</td>
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<td>Germany</td>
<td>1.75</td>
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<td>Italy</td>
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<td>1.86</td>
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<tr>
<td>Netherlands</td>
<td>2.13</td>
<td>1.98</td>
</tr>
<tr>
<td>Slovenia</td>
<td>2.01</td>
<td>2.02</td>
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</tbody>
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Slide from Mark Connolly
On average European women wants 2.0 children – but they only achieve 1.5

Why?
The total fertility rate. A parameter determined by a number of highly complex factors:

Economy
Social factors
Educational demands
Maternity leaves
Availability of child care
Child care costs
Child "bonuses", etc, etc

But to some extent also by the prevalence of infertility......and the efficiency of fertility treatments
Part II. Infertility

1. Infertility and subfertility is defined as > 12 months attempts of pregnancy
2. Primary and secondary infertility.
Pregnancies in fertile and subfertile couples

Probability of conceiving for periods up to 12 months

- Directly after stopping birth control: 84%
- If no pregnancy has been achieved within a year: 49%
- If no pregnancy has been achieved within 3 years: 14%
Surveys on the prevalence of infertility

Prevalence among participants, who have attempted to have at least one child

- Live-time prevalence of infertility (> 1 yrs) 17-26%
- Live-time prevalence of infertility (> 2 yrs) 12-14%
Fertility treatment – Medical and social needs

• Infertility is recognised by WHO as a disease - in the reproductive system
• Primarily infertility is the result of several medical disorders, but it is also dependent on delayed childbearing in the Western culture and to some extend on live-style factors (body-weight, smoking, endocrine disruptors)

Estimate:
• 11 million infertile in Europa (prevalens 9%)
• 50% seek medical assistance
• 22% receive fertility treatments

Facts:
• 480,000 ART treatments annually in Europa
• ~1,000 treatment cycles per million
• NON-ART treatments?


ART public sector
Part III: The postponement of childbirth and fertility

The major change in human reproduction during the last decades
Age at first birth
Denmark 1965-2008

Increase: 1 year/6.4 years

Danmarks Statistik Online: www.dst.dk
Figure 1 Mean age of mother at first birth, selected countries, 1950–2007. Sources: Council of Europe (2006), Human Fertility Database, and own computations based on Eurostat (2009) and national statistical offices.
Number of children – by age of the first child

**Figure 4** Age at first birth and completed fertility rate, Swedish women born in 1935–1939 and 1950–1954. *Source: Andersson et al. (2008: 49, Table 12d).*
Fecundity according to age

Live births per cycle

Couples: 544
Children: 3,846
Post-partum
Amenorrhea: 10 months
Children/woman: 10.8

Larsen U et al. Social Biology 2000; 47: 34-50
Treatments with Donor semen (IUI-D)
Pregnancies/cycle according to age

6,139 IUI-D cycles
1,001 treated women
All during 18 years

Pregnancy and live-birth rates after ART in relation to age. USA 2005

Figure 14
Percentages of ART Cycles Using Fresh Nondonor Eggs or Embryos That Resulted in Pregnancies, Live Births, and Singleton Live Births, by Age of Woman,* 2005

*For consistency, all percentages are based on cycles started.
Pregnancy outcome following ART by woman's age in Australia, 2002-2005

Fertility and age – the ovarian clock

Broekmans et al, Trends in Endocrinology & Metabolism, 2007
Oligo-follicular, small follicle depleted "old" ovary

Multi-follicular, large "young" ovary

AFC = 2
AMH < 3 nmol/l

AFC = 34
AMH = 81 nmol/l
To summarise on age an fertility:

Throughout Europe childbirths are postponed

There is a marked decline in female fertility with age

Late 1. conception is associated to fewer children

We have increased our possibilities to diagnose the decline in "ovarian reserve"
Part IV. Fertility treatments – success and the demographic aspect:

- In several European countries as well as in Denmark the ART professionals as well as the European Society for Human Reproduction and Embryology (ESHRE) have emphasised the demographic aspect of fertility treatments.
- ART provides a small but important contribution in order to increase the birth rates.
- This is of importance for society in a period where Total Fertility Rates (TFR) are much below the replacement levels in Europe – and elsewhere.
§G. "Infertility is one of the causes of demographic decline and it should be recognised as a public-health concern and as a social problem affecting both men and women" and…..

European Parliament report (2007/2156(INI))
“... calls on the Member States to ensure the right of couples to guarantee universal access to infertility treatment and medically assisted procreation by taking steps with a view to reducing the financial and other obstacles."
Focus on REPRODUCTION
European Society of Human Reproduction and Embryology

Crisis?
What crisis?

ESHRE’s role in Europe’s politics of population
ART as a “successful” health technology

Appropriate
Acceptable
Available
Accessible
Affordable

And we could add:

....for all those that could benefit from the technology, based on the concept of equal access for all citizens to health services that is an integrated part of contemporary European thinking
The concept of successful ART programs in a broad perspective

For the infertile population
For the infertile couple
For the clinic

For policy makers
For the obstetrician or pediatrician
For the child
Success in ART

The policy makers
Direct costs (€) per child = 12,000 €
Indirect costs (pregnancy complications, NICU admission and later health support to prematurely born twins) = HIGH €

The obstetrician
Number of vaginal deliveries / all deliveries = 75%

The child
Number of healthy children / all children = 98%
The concept of successful ART programs in a broad perspective

For the infertile population
For the infertile couple
For the clinic
For policy makers
For the obstetrician or pediatrician
For the child
ART cycles / mio in European countries 2007 (Countries with complete recording)

- Denmark
- UK, Germany
- Portugal

ESHRE EIM, Human Reproduction, 2010
Percentage of infants born after ART.
Europe, 2007. (Countries with complete recording)

Countries with public support to ART

- Scandinavia: 3 free cycles
- NL: 3 free cycles
- FR: 4 free cycles
- ES: 3 free cycles

Green = NHS covered or partly covered
Inequalities in the use of ART within countries
No ART clinics in Montana or Wyoming?

Figure 1. Location of assisted reproductive technology (ART) medical centers — United States and Puerto Rico, 2003

Montana
Wyoming

No. of ART medical centers in the United States in 2003: 437
No. of U.S. ART medical centers that submitted data in 2003: 399
No. of ART cycles reported for 2003: 122,872*
No. of live-birth deliveries resulting from ART cycles started in 2003: 35,785
No. of infants born as a result of ART cycles carried out in 2003: 48,756

* This number does not include 163 cycles in which a new treatment procedure was being evaluated.
ART cycles / million in different states
United States

Is ART succesful in Massachusetts?

Cycles/mill.

Wright et al. Surveillance Summaries, 2006, 55, SS-4
Conclusions on Access to ART and the use of ART

- There are huge differences in the accessibility/availability (the use of) ART, between different countries – with similar Gross National Income per capita.

- There are also huge differences within countries.
Consequences of the reduction in re-imbursement to ART treatment in Germany from January 2004.

• Until January 2004:
  4 treatments fully re-imbursed

• From January 2004:
  3 treatments re-imbursed – but only 50% of costs
  (criteria: married couples, female age 24 – 40, husband below 50 years)
The German example
Could ART even be an "investment" for Society?
Direct estimated cost per ARTchild 85,000 DKK (12,000 €)
Why do we see so many ART treatments in a country like Denmark?

- Have tried to reduce costs of ART and simplify procedures to make it available for as many as possible – Make it a ”mainstream treatment”.

- ART included in the National National Health Programs as a standard offer based on strict, simple social criteria.

- Investigation of infertility – a task for the general practitioner.

- Patients have free of charge treatment and roughly 75% of all medicine costs re-imbursed

- Specialised independent ART units distributed geographically to cover all regions

- Have a mixture of a public and a private sector (50-50%)

- ART have been regulated. There is confidence in ART in the population. Confidence that tax payers money are spent resonably.
Criteria for free of charge public ART in Denmark

- Medically indicated
- Female age below 40 years
- No children in the marriage (relationship)

- Single women and lesbians allowed treatment also with ART – if IUI-Donor has failed
Independent specialised ART units

• The public clinics are typically independent and highly specialised in ART (not general gynecological functions).
  
  We do not take "smears"
  Surgery (endometriosis, myomas, adherences) – done by collaborating gynecological departments

• Separate budgets, separate personel, 7 days a week.
  
  Infertility patients are thus given full priority at the unit

The net effect – efficient flow of ART treatments
What would the real need for ART be if all couples should have the full benefit of the technology?

The present use of ART in Europe and North America (generally < 1000/mio) is much lower than the optimal (from a strict medical point of view) which is 5-8,000 treatments per million - if all couples who fail non-ART treatments should have the full benefit of ART, which is up to 6 cycles.

"International estimates of infertility prevalence and treatment-seeking: potential need and demand for infertility medical care"

Finally - What to do?

• We can start systematic initiatives to inform the public about ”protection of fertility”
• Fertility counselling clinics? (like contraceptive clinics 40 years ago)
• We can strengthen general preventive measures
• We can assure the accessibility of ART and non-ART treatment to the infertile population
Thank you for your attention