

NATURAL CYCLES in low resource countries

Has it a place?

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ESHRE Campus From natural cycle to minimal stimulation Maribor 27-28 February 2009
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Synthesis

27. February 2009

12.00 - 12.30	Preparatory topics: last and ultra-minimal stimulation in natural cycle
	A. Vlahopoulos (Greece)
12.30 - 13.00	Is natural cycle IVF effective and cost effective?
	G. Hargreave (United Kingdom)
13.00 - 13.30	Natural cycle as a means of increasing access to ART in developing countries
	W. Dombaut (Belgium) (TBC)
13.30 - 14.00	Modified natural cycle: the best of both worlds?
	M. de Boer (The Netherlands) (TBC)

28. February 2009

09.00 - 09.30	What did we learn from the review of 1200 natural cycles for fertility?
	M. Vogel (Germany)
09.30 - 09.45	Serum and follicular hormonal profile in natural IVF cycles
	V. Bokal Brackic (Slovenia)
09.45 - 10.00	Natural IVF cycle with and without HCG administration
	H. Bormann (France) (TBC)
10.00 - 10.20	Natural IVF cycles in poor responders or ovulation induction problems
	E. Tombalova (Greece)

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objectives

- Identify unresolved issues in low resource countries
- Review and assess recent developments in NC
- Provide recommendations for practice

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Low resources or developing countries



developing

developed



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What is determinant ?

• National Income

• Gross Domestic Product – GDP

measures the value of economic activity

• Gross National Product – GNP

*Converted into US dollars at the official exchange rate
Divided by the country population - this gives an
average figure for GNP per head*

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GDP per capita

• below average



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Percent poverty world map



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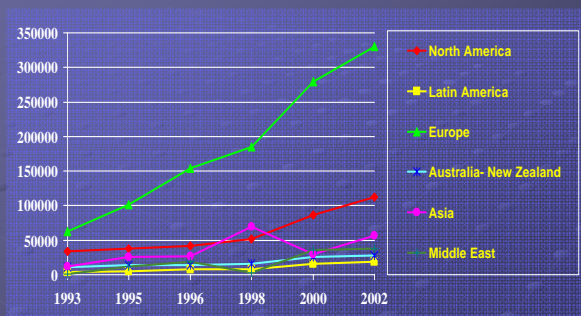
demography of fertility & infertility

- regional differences
- Africa has much higher level of fertility in than in other regions
 - it is surprising to observe that contrary to expectation
- The level of *infertility* is higher in Africa than elsewhere
 - measure of infertility is
 - proportion of women who are childless by the age of
 - 40 to 44 years
 - 45 to 49 years
 - at the end of their fecund period of life.
- Substantial variation between countries and within regions
 - women in their forties who are childless in Africa ranges from
 - a level of a few percent in western Africa,
 - to
 - third of women in central Africa



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Evolution of ART Cycles by Region



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Availability per country

Cycles/million	Births/1000	Cycles/million	Births/1000
Israel 3153	Netherlands 46.3	Ireland 408	New Zealand 8.7
Denmark 2050	Denmark 43.4	New Zealand 419	Ireland 8.0
Finland 1388	Slovenia 34.7	USA 413	Bahrain 3.5
Cyprus 1174	Israel 34.2	Lithuania 317	Poland 3.2
Australia 1191	Iceland 30.1	Poland 127	Macedonia 2.6
Slovenia 1188	Sweden 29.3	Argentina 119	Libya 2.3
Ireland 1179	Finland 26.5	Macedonia 115	Uruguay 1.9
Norway 1175	Cyprus 26.4	Uruguay 101	Argentina 1.5
Germany 1073	Norway 23.9	Russia 89	Chile 1.2
France 1053	Germany 21.9	Brazil 66	Russia 1.0
Netherlands 987	Australia 19.2	Chile 65	Brazil 0.9
Norway 810	Hungary 18.7	Venezuela 41	Venezuela 0.5
Switzerland 715	France 15.4	Syria 32	Peru 0.2
Hungary 683	UK 13.7	Peru 23	Syria 0.1
Norway 640	Switzerland 13.5	Ecuador 9	Ecuador 0.1
UK 611	Croatia 12.3	Dominic Rep 2	Guatemala 0.02
Croatia 582	USA 10.0	Guatemala 2	Dominic Rep 0.01

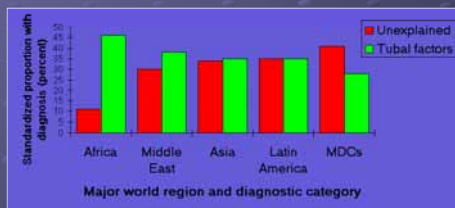
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Major cause of excess infertility

● acquired sterility due to pathological conditions

especially notable in Africa

- tubal infertility nearly 64%
 - sexually transmitted diseases have prominent role
 - availability of medical and therapeutic interventions
- ovarian or endocrine disturbances 24%



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Method of choice ? IVF

● Why IVF

- Dominance of Tubal factor:
- STDs

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**Factors Involved In Infertility treatment
in developing world**

- Social
- Cultural
- Economic
- Demographic
- Ethnic
- Religious

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Factors involved in infertility in developing countries

- Negative consequences of childlessness are much stronger
- Prevention and alternative methods are not always successful
- Adoption is not an option in most DC (socio-cultural, religious)
- Equity: IVF should not only be available for the rich
 - Possibility of
 - simplifying diagnostic procedures
 - simplifying clinical procedures (IVF-cycle)
 - simplifying laboratory procedures (IVF)
 - opportunity of establishing 'Reproductive Health Care Centres' with possibilities for family planning/mother-care/infertility diagnosis & treatment

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**obstacles in infertility treatment in low resource
countries**

- Infertility diagnostics
- Treatment feasibility and costs
- Preventive measures – how and consequences of low prevention level in low resource countries

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Aims of IVF service in developing countries

- Cost
- Visits
- Monitoring
- Complications
- Stress

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NC & terminologies used in the literature

Recommended	To replace
Natural cycle IVF	Unstimulated, spontaneous cycle IVF
Modified natural cycle IVF	Semi-natural, controlled natural cycle IVF
Mild IVF	Soft, minimal stimulation, 'friendly' IVF
Conventional IVF	Standard, routine IVF, controlled ovarian stimulation IVF

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Definition simplified and revised nomenclature

Terminology	Aim	Methodology
Natural cycle IVF	Single oocyte	No medication
Modified Natural cycle IVF	Single oocyte	hCG only Antagonist & FSH/HMG add back
Mild IVF	2-7 oocytes	Low dose FSH/HMG, oral compounds & antagonist
Conventional IVF	≥ 8 oocytes	Agonist or antagonist conventional FSH/HMG dose

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Advantages of NC IVF

Systematic literature review (20 selected studies)

Painick et al Hum Rep Update 2002

- 1800 natural cycles
 - Embryotransfer rate 45%
 - Pregnancy rate per cycle 7.2%
 - Pregnancy rate per transfer 15.8%
- Cancellation of CPU
 - Ovulation triggering with HCG rate of oocyte retrieval per cycle 67.3%
 - Timing of spontaneous LH surge rate of oocyte retrieval per cycle 80.6%
- Oocyte recovery rate 88.6%
- Fertilisation rate
 - IVF cycles 44.2-100%
 - ICSI cycles 56.3-62.5%

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Factors affecting pregnancy success of IVF in NC

- Patient age
- Indications for IVF
- Previous IVF treatment
- Baseline value of FSH, LH, PRL
- Embryo, oocyte and semen quality
- Endometrial thickness
- Day of ET
- Serum E2 level on day of hCG

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NC IVF success rates

- Accurate monitoring
- Selection of patients
- Method: IVF or ICSI
- Embriootransfer: day 2 or day 5?
- Influence of patients age
- Luteal supplementation

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AIM

- ART should be designed to be robust, repeatable and efficient
- Equipment should be basic, sturdy and strong
- Products should be solid, ready to use and with a long half-life
 - Sperm processing materials are best aseptically packaged (set or kit) and stored at room temperature
 - Embryo culture media should be robust, short-term, pre-packaged in small quantities
 - Disposables (pipette tips, screening dishes) can be pre-packaged as 'a set per patient'
- Information to the community should be discrete and applicable, taking into account sociocultural and religious differences
- A training program (with follow-up/audits) for the medical and paramedical staff should be designed.

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But little is known about

- Real cost/benefit score in ART/IVF
- Minimal costs for IVF in:
 - Different countries worldwide
 - Low-resource countries
- Future possibilities to get:
 - Cheaper medication
 - Low-cost equipment

Component	Cost (USD)
1. ART Procedure (including lab fees)	10,000 - 15,000
2. Medication (including hormones)	2,000 - 5,000
3. Support system (including nursing)	1,000 - 2,000
4. Medical device (including ultrasound)	500 - 1,000
5. Knowledge (including training)	100 - 200
6. Procedure (including lab fees)	100 - 200
7. Support system (including nursing)	100 - 200
8. Medical device (including ultrasound)	100 - 200
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100. Medical device (including ultrasound)	100 - 200

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ART technology - Regional differences

- Knowledge
- Equipment
- Medical Device
- Drugs
- Procedure
- Support system



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YES

as it has a place in
developed countries but...

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