The Arusha Project

Willem Ombelet
Barcelona 03-11-09 / 36th International Symposium
Continuum of consequences of infertility

Level 1: Fear, guilt, self-blame

Level 2: Marital stress, Depression, helplessness

Level 3: Mild marital or social violence, Social isolation

Level 4: Social isolation, Violence-induced suicide, Starvation / disease

Level 5: Total loss of social status, Severe economic deprivation, Moderate to severe violence

Level 6: Lost dignities in death
Third World = overpopulation

ART = ethical issue

Limited budget

1st priority = Education Family-planning

ART = expensive

More important priorities: HIV, tbc, malaria, vaccinations ...

Task n°1 = Prevention Education

Limited or no interest for infertility in developing countries
Patient // Society - friendly ART

- Cost – effectiveness
- Access
- Risk minimisation
- Burden minimisation

Make it
SIMPLE
EFFICIENT
SAFE
AFFORDABLE
Strategies to simplify IVF

Natural cycle
Clomiphene citrate
Low dose hMG / rec FSH
Monitoring: (only) ultrasound
Single Embryo Transfer
Laboratory - technics
Laboratory - material

IUI as a first line treatment

Natural cycle
Clomiphene citrate
hMG or rec FSH: minimal dose step-up regimen
Algorithm for male subfertility treatment

- Tubal Factor
  - No Tubal Factor
    - Initial Semen Sample
      - Washing procedure
        - IMC < 1 million
          - Morphology < 4% → ICSI
          - Morphology >= 4% → IVF
        - IMC >= 1 million
          - Morphology < 4% → ICSI
          - Morphology >= 4% → IVF
      - Washing procedure
        - IMC < 1 million
          - Morphology < 4% → ICSI
          - Morphology >= 4% → IVF
        - IMC >= 1 million
          - Morphology < 4% → ICSI
          - Morphology >= 4% → IVF

< 30% or no fertilisation
Infection-related tubal factor

Third World
- 32%

Asia
- 39%

Latin America
- 44%

Africa
- 65 - 85%

Tubal factor: why?
- Sexually transmitted diseases
- Post-partum infections
- Illegal abortions
- Urbanisation - mobility
- Polygamy
- Resistant micro-organisms...
Problem of accessibility

Population: 1,000,000

100,000
10% Cohabiting woman (18 - 44 year)

90% fertile
10% infertile

10,000

50% conservative

50% seek infertility care

5,000

40% Pregnant without IVF (Spt, Non-IVF, after surgery,....)

60% IVF selection

3,000

50% Need IVF

50% Refuse IVF

1,500

Assumed need for IVF / ICSI = 1,500 / year / million
Fauser et al, Hum Reprod Update, 8, 1, 2002

Nigeria
> 190,000 cycles per year
Arusha (expert) meeting
ESHRE STF “Developing countries & infertility”
December 15-17, 2007

37 participants

President-elect ESHRE
Past president ESHRE
Past-president IFFS
President-elect FIGO
President MRSM
Principal advisor President Museveni (Uganda)
Representative of EC
Representative of WHO
President ISMAAR
**4 Working Groups (WG)**

- **The one-day diagnostic phase**  
  R Campo

- **Ovarian stimulation for IUI & IVF/ICSI**  
  AN Andersen

- **Laboratory phase for IUI & IVF/ICSI**  
  J Van Blerkom

- **Fundraising**  
  H Sallam

**5 Study Groups (SG)**

- **Reproductive health education, prevention & awareness**  
  G Serour

- **Burden of disease & cost-effectiveness**  
  D Habbema

- **Training courses**  
  I Cooke

- **Intravaginal // intrauterine culturing**  
  R Frydman

- **Differences in ethics / law / religion / level of care**  
  F van Balen
| Level 1 | basic infertility exploration  
treatment options: up to IUI |
|--------|-------------------------------|
| Level 2 | + diagnostic laparoscopy  
treatment options: up to IVF |
| Level 3 | + operative endoscopy  
treatment options: ICSI & cryopreservation |
| Level 4 | + ?? |

1. Equipping the clinics  
2. Training the staff  
3. Educating the public  
4. Running the services
Accessible ART services

Diagnostic phase

Ovarian stimulation

Lab phase
One-day clinic (diagnosis)

Female

Clinical examination
Blood sample: Hb, Hep B, Hep C, HIV
cervical smear
TB-testing
Hystero-salpingography
Vaginal ultrasound
PCT if regular cycle & easy access to centre
Optional: mini-hysteroscopy

Male

Clinical examination
Blood sample: Hep B, Hep C, HIV
TB-testing
Semen examination: fresh sample
Count & motility a + b
After washing: IMC (& morphology)
Good Quality-Low Cost Ultrasound

£ 6500 or 7400 Euro

Chinese company

Mindray DP-6600 with 2 probes
Accessible ART services

Diagnostic phase

Ovarian stimulation

Lab phase
Natural cycle IVF systematic review – 1800 cycles

- Complication rate (MPR & OHSS): almost zero
- Much cheaper
- ET per cycle: 45.5%
- Ongoing pregnancy rate per cycle: 7.2%
- Ongoing pregnancy rate per transfer: 15.8%

Reason: premature LH rise / ovulation

→ need for randomized controlled trials

Pelinck et al., HR Update, 8, 129, 2002
Low-cost IVF stimulation

- Clomiphene 100 mg
- hCG 5000U

MENSES

- U.S. OVARIES
- >= 17 mm
- x
- x+1

35 h

Price
- Medication
- 13 Euro

Price
- Medication
- Belgium per cycle
- 1000 Euro !!
## Monitoring ART treatment

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Ultrasound Examinations</th>
<th>Biochemical Testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>IUI</td>
<td>max 2 US</td>
<td>no biochemical testing</td>
</tr>
<tr>
<td>IVF</td>
<td>max 2 or 3 US</td>
<td>no biochemical testing</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 x urinary LH</td>
</tr>
</tbody>
</table>
INNER CHAMBER

OUTER RIGID SHELL
**Make it SIMPLE EFFICIENT SAFE AFFORDABLE**

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**TRANSPORTABLE INCUBATORS**

Specimen tubes of various dimension to suit most applications can be accommodated in the thermally conductive blocks.

The BioTherm™ INC-RB1 is supplied with two blocks as standard. Currently, six block models are available to choose from. Custom Blocks can also be made. These can be removed by the user to clean or interchange.

The same range of block styles are available as fixed cores in the BioTherm™ INC-12V. In addition, a straw cassette is available with a fixed core as shown.

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**STANDARD BLOCKS & CORES**

- **A12-1**
  - 12 Microtubes (1.5mL Ø x 94mm)
  - 1 x 14ml or 15ml Tube (12mm Ø x 63mm)
- **F6/6**
  - 6 x 14ml or 15ml Tubes (17mm Ø x 96mm)
  - 6 x 5ml or 6ml Tubes (12mm Ø x 63mm)
- **L14/14**
  - 14 x 1.8ml Cryovials (13mm Ø x 14mm)
  - 34 x Auto-sample Tubes (8.5mm Ø x 98mm)
- **G17**
  - 17 x 5ml or 6ml Tubes (12mm Ø x 63mm)
- **V12**
  - 12 x 10ml Tubes (16mm Ø x 92mm)
- **E10**
  - 16 x 14ml or 15ml Tubes (17mm Ø x 96mm)
- **SC 8/1**
  - 8 x 5ml or 6ml Tubes (12mm Ø x 63mm)
  - 1 x 14ml or 15ml Tube (12mm Ø x 97mm)
  - 1 x Cassette Slot (136mm x 94mm x 13mm)

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**Specifications**

**12V / RB-1**

- Selectable Temperature Range: 32.5°C to 40.0°C
- Temperature Steps: 0.5°C
- Holding Time: > 30 hours at 40°C, battery fully charged
- Thermal Fuse Trip Point: 59°C
- Batteries: 2 x 6V x 4Ah, sealed lead acid
- Battery Dimensions: Typical 70x46x105 (WxDxH) mm
- External Dimensions: 275 x 212 x 258 (WxDxH) mm
- Weight: 6kg (including batteries)

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**CryoLogic**

Innovative Instrumentation
Action Plan – Objective & background
(J Van Blerkom)

- Minimalist approach – back to basics
- Avoid needless complex instrumentation / reagents ..
- Simple incubation system – single temperature (37°C)
  - Battery

Non-CO₂ based culture conditions
- Less oocytes / embryos
- 24 – 36 culturing
- Culture medium: simple // for 1 – 2 days
- Looking for pronuclear characteristics / mononucleation / blastomere symmetry
Cost /cycle/ 100 per yr.

- Fixed cost: $18,200 /500 = 36 / cycle
- Consumables: 265
- Overhead: 20

$321 = 254 Euro

+ personnel !!!!

A De Cherney, Geneva 2008
## Income /// health care costs in DC

<table>
<thead>
<tr>
<th>Country</th>
<th>Daily income % &lt; 1 $</th>
<th>Daily income % &lt; 2 $</th>
<th>Health care % of GNP</th>
<th>Health care % out of pocket</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tanzania</td>
<td>90 %</td>
<td>58 %</td>
<td>4 %</td>
<td>83 %</td>
</tr>
<tr>
<td>India</td>
<td>80 %</td>
<td>35 %</td>
<td>5 %</td>
<td>94 %</td>
</tr>
<tr>
<td>Indonesia</td>
<td>52 %</td>
<td>8 %</td>
<td>3 %</td>
<td>75 %</td>
</tr>
<tr>
<td>China</td>
<td>47 %</td>
<td>16 %</td>
<td>5 %</td>
<td>86 %</td>
</tr>
<tr>
<td>Brazil</td>
<td>21 %</td>
<td>8 %</td>
<td>9 %</td>
<td>64 %</td>
</tr>
</tbody>
</table>
Pilot-project for LC-IVF

Suggested centre

Egypt: Alexandria
Selection of patients / methods

- Only childless women
- Age limits:  
  Women: > 18 & < 35 yrs  
  Male: < 55 yrs
- only IVF (no ICSI)
- SET or DET
Future activities if phase 1 is successful

Implementing more level 1 centres

Implementing more level 2 centres

Implementing level 3 centres

→ Registration obliged – yearly audit (ICMART)
Training courses
(ESHRE, IFFS)

- different packages (level 1 – 3)
- Manual & protocols for each level
- train the trainees
  - Diagnostic phase (ISMAAR, EAGE ...)
  - Clinical aspects IUI & IVF cycles
  - Laboratory phase IUI & IVF/ICSI
Funding the project

**ESHRE**
training courses / website / secretarial support

**Walking Egg Project NPO**
secretarial support - project manager
funding – campaigns (affordable art)

**WHO**
Leaflets
Implementing infertility services

**Fertility centres -- solidarity**
1 euro or $ per cycle

**Other foundations**
Bill Gates & others

**Governments**
**EC - United Nations**
**African World Bank**
World Community Statements

1. “Men and woman of full age, without any limitation due to race, nationality or religion, have the right to marry and to raise a family”. This statement was adopted 60 years ago at the 1948 UN Universal Declaration of Human Rights and can’t be misunderstood: it implies the right to access to fertility treatments when couples are unable to have children.

2. At the United Nations International Conference on Population and Development in Cairo in 1994 the following statement was made “Reproductive health therefore implies that people have the capability to reproduce and the freedom to decide if, when and how often to do so … and to have the information and the means to do so …”


4. In 2001, on the occasion of a WHO meeting on "Medical, Ethical and Social Aspects of Assisted Reproduction" in Geneva, a call for the integration of infertility into existing sexual and reproductive health care programmes in developing countries was made.

5. In 2004 the World Health Assembly proposed five core statements, including “the provision of high-quality services for family-planning, including infertility services”.

6. At the World Summit in 2005, the largest-ever gathering of world leaders called for achieving these goals by the year 2015.

7. At the Oslo Ministerial Declaration in 2007 health was recognised as one of the most important long-term foreign policy issues by the Ministers of Foreign Affairs of Brazil, France, Indonesia, Norway, Senegal, South Africa, and Thailand. “The well functioning health systems that are needed to reduce maternal newborn and child mortality and to combat HIV/AIDS, tuberculosis and malaria will also help countries to cope with other major health concerns such as sexual and reproductive health ...
30 years IVF

> 3 million IVF / ICSI babies

SUCCESS !!! (??)