Recent Progress and Problem of Reproductive Medicine in JAPAN

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Where is Tokushima City in Japan?

Japan
120 million

Shikoku Island
4 million

Tokushima city
0.3 million

Traditional Folk Dance
“Awa Odori”

Vortex in the Naruto Strait

Traditional puppet show
Music bands in the camp played the Ninth Symphony of Beethoven on June 1st in 1918 for the first time in Japan. Since then, Beethoven's 'the Ninth' has been played on the first Sunday in June annually in Naruto.

Bando POW Camp that existed during WWI, from 1917 to 1920 in Bando, Naruto, Tokushima. This is the place where approximately 1,000 German POWs lived in relative freedom.

The Naruto German House
Tokushima University

Graduate School of Biomedical Sciences is made up of 3 schools, Institute of Basic Medical Sciences and University Hospital
Today’s TOPICS

Ⅰ. Annual reports of Japan Assisted reproductive Technology (ART) registry (1983-2014)

Ⅱ. Japanese Society for Obstetrics and Gynecology (JSOG) Guidelines for Ethics Policy in Reproductive Medicine
Ⅰ．Annual reports of Japan Assisted reproductive Technology (ART) registry (1983-2014)
The number of ART cycles has increased.

- Cryo: Cryopreservation + Embryo Transfer (ET)
- IVF: Fresh ET
- ICSI: Intracytoplasmic sperm injection + ET
# of Birth has increased in this decade
(cryo-baby rate: about 80%)

Cryo IVF ICSI

Japan ART Registry 2014
Success rate of ART

- Pregnancy/Cryo ET
- Pregnancy/Fresh ET

Japan ART Registry 2014
Summary #1
Annual reports of Japan ART registry shows

**Attempted treatment cycles** 393,745

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<tr>
<th>Procedure</th>
<th>Count</th>
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<tr>
<td>ART clinics</td>
<td>598</td>
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<tr>
<td>Oocyte Aspiration cycles</td>
<td>231,285</td>
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<tr>
<td>Fresh ET cycles</td>
<td>71,850</td>
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<tr>
<td>Cryo ET cycles</td>
<td>153,868</td>
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<td>Delivered babies</td>
<td>46,017</td>
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- **Japan is a country of largest number of ART treatment in the world**
- **ART booming among more than 40yo.patients.**
- **Elective “Cryopreservation ET” have been increased and 80% of delivered babies were by cryoET**
II. Japanese Society for Obstetrics and Gynecology (JSOG)
Guidelines for Ethics Policy in Reproductive Medicine
Every country has every ethics policy which regulates ART

- Law
- Government guideline
- Academic guideline

- In Japan, ART is supervised by Academic guidelines
Various JSOG Guidelines for Ethics policy in reproductive medicine

- ART clinic registration
- ART annual report
- ICSI policy
- Cryopreservation of ART
- Artificial insemination with donor sperm (AID)
- Avoidance of multiple pregnancy
- Clinical research policy for ART
- Basic research policy using embryo and died babys Organs
- Preimplantation genomic diagnosis
- Oocyte, sperm and embryo donation policy
- Gamete cryopreservation technics for patient with malignant disease
Consideration on many factors in decision of JSOG ART Policy

- Client request
- Developing level of technology
- Avoidance of commercialism
- Clinical usefulness
- Clinical necessity
- Women’s right
- Ethics
- Japanese traditional Culture
- Law for family system
Ethics of reproductive medicine is specific and complicated.
JSOG single embryo transfer (SET) Policy started in 2008 with JSOG guideline

34 y.o. or younger
- 1st: SET
- 2nd: SET
- 3rd: SET or DET
- 4th: SET or DET

35 y.o. or elder
- 1st: SET or DET
- 2nd: SET or DET
- 3rd: SET or DET
- 4th: SET or DET

( no transfer with 3 or more embryos )
Change of % of SET (2007-2014)

Japan ART Registry 2014
% of multiple pregnancy in ART

Multiple pregnancy rate of ART decreased by JSOG SET policy

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<td>Rate</td>
<td>17.2%</td>
<td>11.5%</td>
<td>5.1%</td>
<td>4.7%</td>
<td>3.7%</td>
<td>3.2%</td>
</tr>
</tbody>
</table>

JSOG SET policy started

Japan ART Registry 2014

17.2% in 2001
11.5% in 2007
5.1% in 2009
4.7% in 2010
3.7% in 2012
3.2% in 2014
JSOG Ethics Committee have had discussions on new guideline as below:

- Preimplantation Genomic Test
- Gamete and embryo donation and IVF surrogacy
Preimplantation Genomic Test (PGT)

- **Preimplantation Genomic Test for Monogenic**
  (PGT-M: Check one specific abnormality of chromosome)

- **Preimplantation Genomic Test for Aneuploidy**
  (PGT-A: check the abnormality of number of chromosome)
Present JSOG policy for PGT

- We carry out only PGT-M as clinical research trial
- Ethics Committee must review every PGT-M cases
- We permit PGT-M for two targets
  1. Serious genomic disease without appropriate treatment
  2. Recurrent Spontaneous abortion due to genomic factor
- PGT-A is prohibited in ART
Why PGT-A prohibited in the present? There are many ethics opinions on PGT in Japan

**Agreement**

- Decrease serious genetic disease
- Decrease miscarriage rate of pregnancy
- Increase ART successful rate

**Non-agreement**

- Can check whole genomic information
- Pregnancy Termination is easily performed
- No reviewed data for usefulness of this technology
Pregnancy and miscarriage rates of ART

Japan ART Registry 2014
Age-distribution of ART cases in 2007 and 2014

Japan ART Registry 2014
Recently there has been a rapid shift to late marriage and late child-bearing in Japan and abnormal pregnancy increased.

PGT technology has rapidly developed (biopsy techniques and examination methods as microarray or New Genomic Sequencer).

Clinical trial has been performed in Europe and USA
① High age patient (more than 37 years old)
② Recurrent miss ART (more than 3)
③ Recurrent spontaneous abortion
④ Serious male factor
⑤ Past history of abnormal baby
We must arrange the environment of PGT-A before JSOG PGT policy will be changed to permission.

- Study for evaluation of the effect of PGT-A
- Discussion for ethics problems which are pointed out by non-agreement opinions
Government supports (to make a low) is necessary in ART medicine using donation with egg and sperm and IVF surrogacy

- National regulating system is necessary

- Definition of “who is mother” in Japanese law →”The Mother” will be the women who has child-bearing

- Prohibition of Commercialism for donation and ART surrogacy with punishment

- Keeping baby’s the priority of origin
Summary #2
What is necessary in order to introduce new ART technology?

- A lot of ethics factors must be discussed
- National consensus including ethics and law
- Avoidance of commercialism
- Suitable and proper information for client patients
Acknowledgment

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