

Medical Aspects of Assisted Reproductive Technology

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Objectives

- Review key features of therapy
- Point out aspects of therapy relevant to our discussion
- Summarize the impact of the technology

Definition of ART

- All treatments or procedures that involve surgically removing eggs from a woman's ovaries and combining the eggs with sperm to help a woman become pregnant.
 - <http://www.cdc.gov/ART/ART2004/appixb.htm>

Key Components of Therapy

- Ovarian stimulation
- Egg (sperm) retrieval
- Fertilization in vitro
 - Intracytoplasmic sperm injection (ICSI)
- Embryo culture
 - Preimplantation genetic diagnosis (PGD)
- Embryo transfer
- Embryo cryopreservation

Ovarian Stimulation

- Principle: maximize the yield of fertilizable eggs
- Practice: several hormonal drugs injected daily or twice daily for 1-4 weeks
- Effect: ten-fold increase in egg production

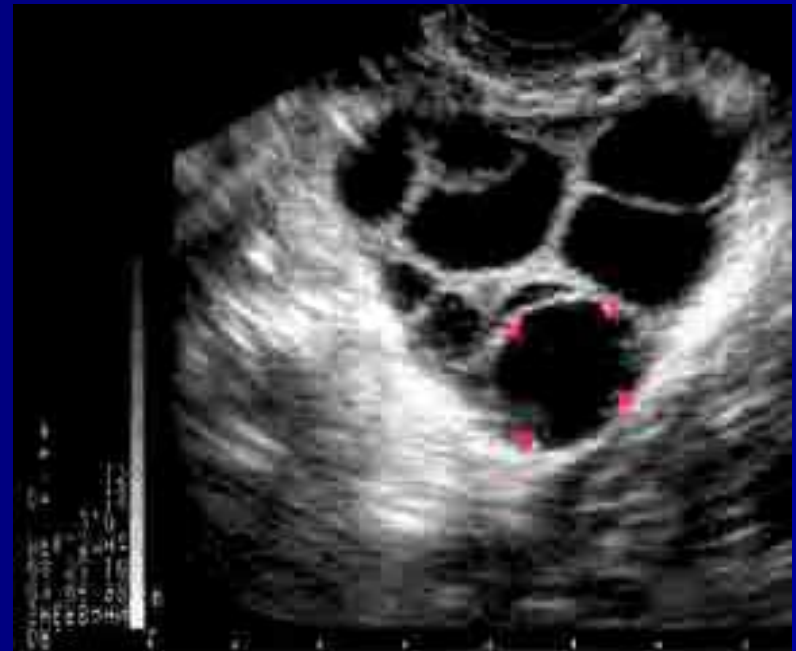
Impact of Ovarian Stimulation

- Bourne Hall 1981: one in five egg retrievals failed to yield an egg
- Australia 1983: one in four egg retrievals produced an ongoing pregnancy
- Australia 1983: 35% multiple pregnancy rate (25% twins, 5% triplets)

Sample Stimulation

- Oral contraceptive pills (OCPs) for 21 days
- Start daily Lupron® injections on 16th day of OCPs
- Start daily injections of FSH on 3rd day of menstrual period
- Measure follicle growth and serum estradiol levels frequently
- Administer hCG when mature follicles are developed

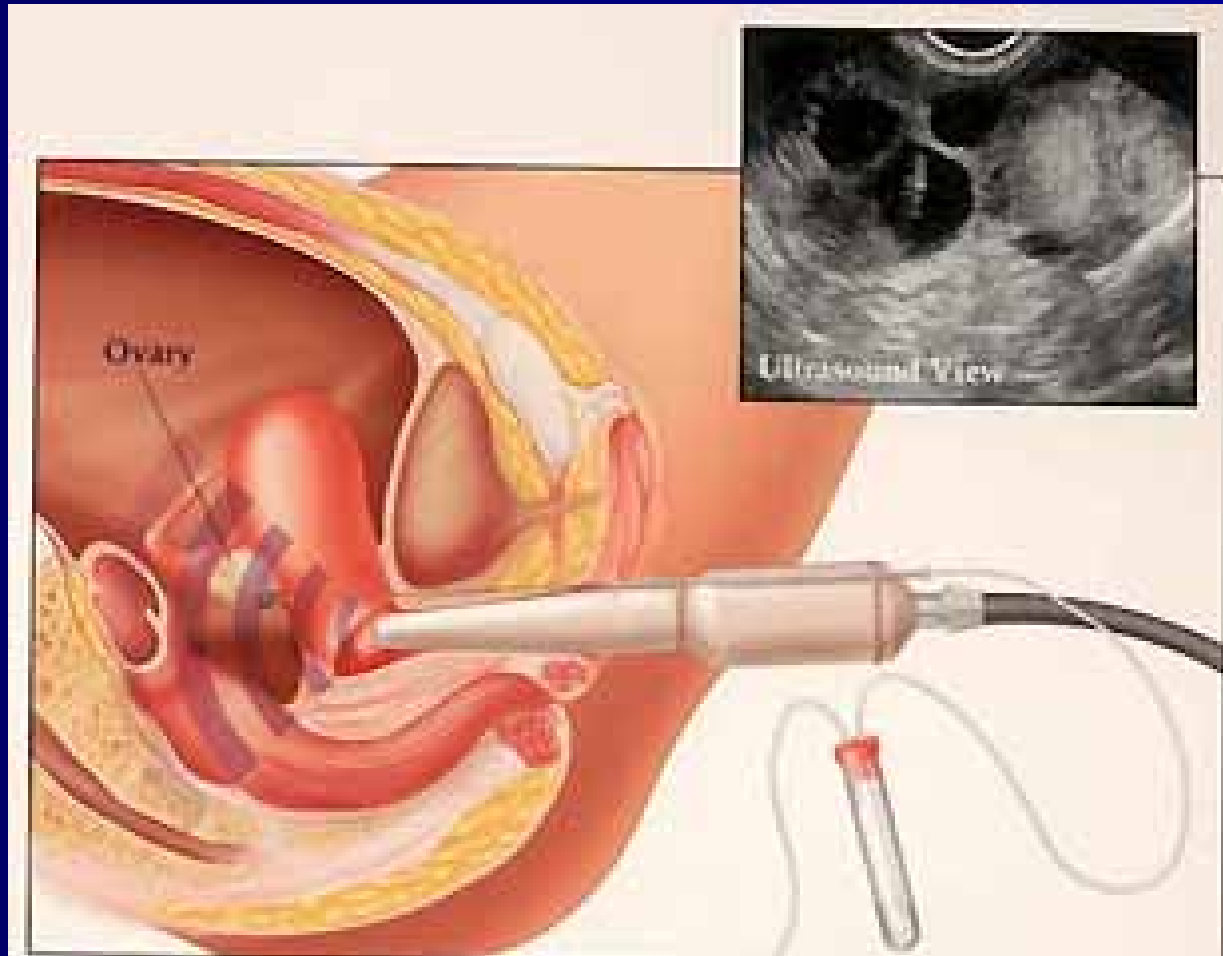
Ultrasound monitoring



Egg and Sperm Retrieval

- FEMALE: Needle aspiration with vaginal ultrasound guidance in outpatient surgery or office setting
- MALE: masturbation or microsurgical exploration of male reproductive organs

Egg Retrieval



In Vitro Fertilization

- Mixing of purified sperm preparation with isolated eggs in a controlled laboratory environment
- Injection of single sperm into the egg cytoplasm (ICSI)



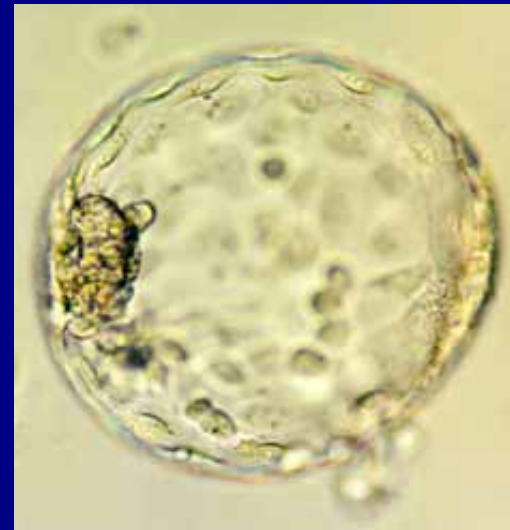
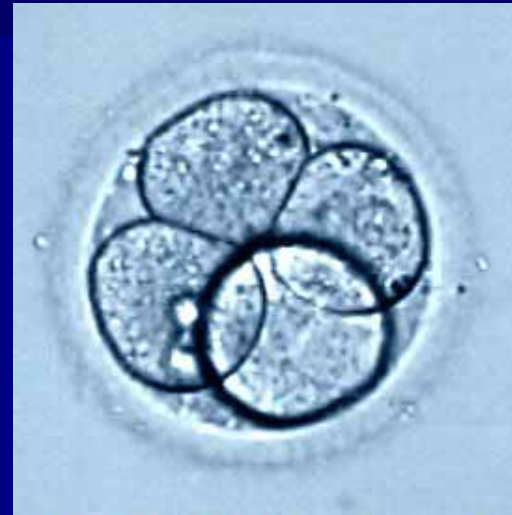
ICSI

- First successful application in 1992
- ICSI expanded the use of IVF for severe male factor
- Motivated urologists to refine surgical techniques for sperm retrieval
- Now widely used even in absence of male factor (58% of IVF cycles in 2004)

Embryo Culture

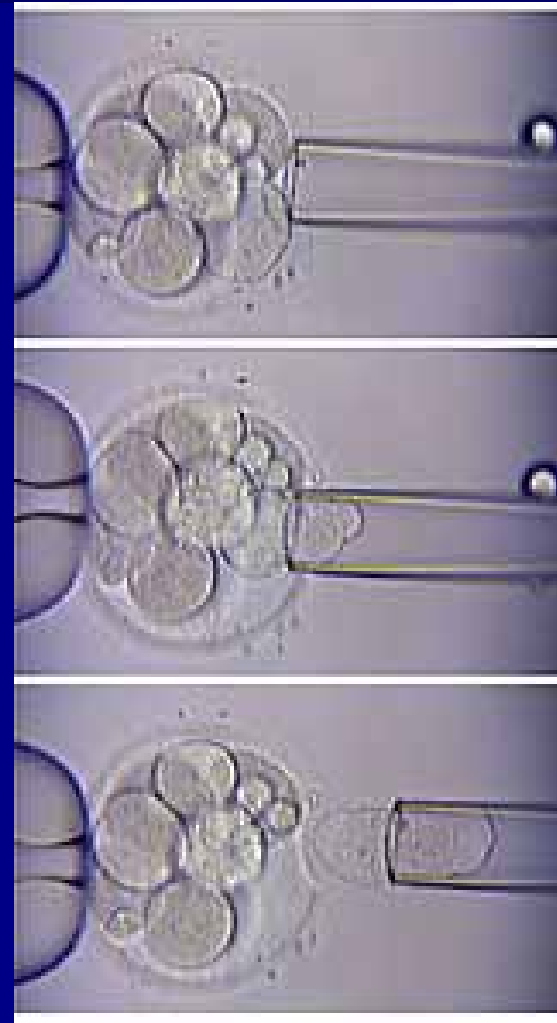


Embryo Development



Preimplantation Genetic Diagnosis

- Microsurgical removal of cell on Day 3
- Probe cell with fluorescent markers for chromosomes
- Extract DNA and probe for gene mutations
- Transfer normal embryo(s) on Day 5



Embryo Transfer

- Selection of “best” embryo(s) to transfer
- Insertion of fine plastic catheter into the uterus through the cervix

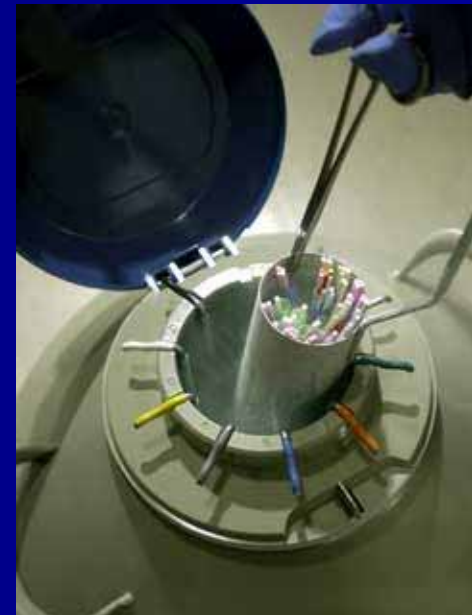


Post-Transfer

- Hormonal supplements to support uterine function (progesterone)
- Serum pregnancy test about 12 days after embryo transfer

Embryo Cryopreservation

- First successful case in 1983
- Requires use of cryoprotectant solutions and specialized equipment
- Stored in liquid nitrogen containers
- Duration of storage practically unlimited
- Estimated 500,000 frozen embryos in the US



Frozen Embryo Transfer

- US Data indicates lower success rates from transfer of frozen/thawed embryos (28% live birth rate versus 34% for fresh embryos)
- Responsible for over 6000 babies in 2004
- Cost and treatment burden significantly less than IVF

Patient Selection

- Infertility: inability to conceive after one year of exposure
- Irreparably damaged tubes
- Failed other fertility treatments
- Severe sperm abnormalities

US Data on Patient Diagnoses

Tubal factor	11%	Other factor	8%
Ovulatory dysfunction	6%	Unknown factor	11%
Diminished ovarian reserve	12%	<i>Multiple Factors:</i>	
Endometriosis	6%	Female factors only	12%
Uterine factor	1%	Female & male factors	18%
Male factor	17%		

SOURCE:

<http://apps.nccd.cdc.gov/ART2004/nation04.asp>

Utilization of ART

- Infertility estimated to affect 7% of married couples of reproductive age (2.1 million couples)
- 127,977 ART cycles in 2004
- 2002 international survey:
 - Average utilization 289 cycles/million population
 - US utilization 126 cycles/million

Current Status of ART

- Responsible for 49,458 infants in 2004 (1% of US births)
- Responsible for 16% of twins and 45% of triplet births
- Responsible for 500K frozen embryos
- Sources:
 - <http://www.cdc.gov/art/ART2004/index.htm>
 - Dickey RP. Fertil Steril 2007 May 2 [Epub]

Summary

- ART is an expensive, resource intensive therapy
- ART has dramatically altered the landscape of fertility therapy
- ART has created new challenges for society