Infertility, In Vitro Fertilization (IVF) and Genetic Testing

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HRC
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HUNTINGTON Reproductive Center
MEDICAL GROUP
REPRODUCTIVE ENDOCRINOLOGY & INFERTILITY

Do you have any friends or family members that have struggled with infertility?

a. Yes

b. No

Do you think that you are fertile?

a. Yes
b. No

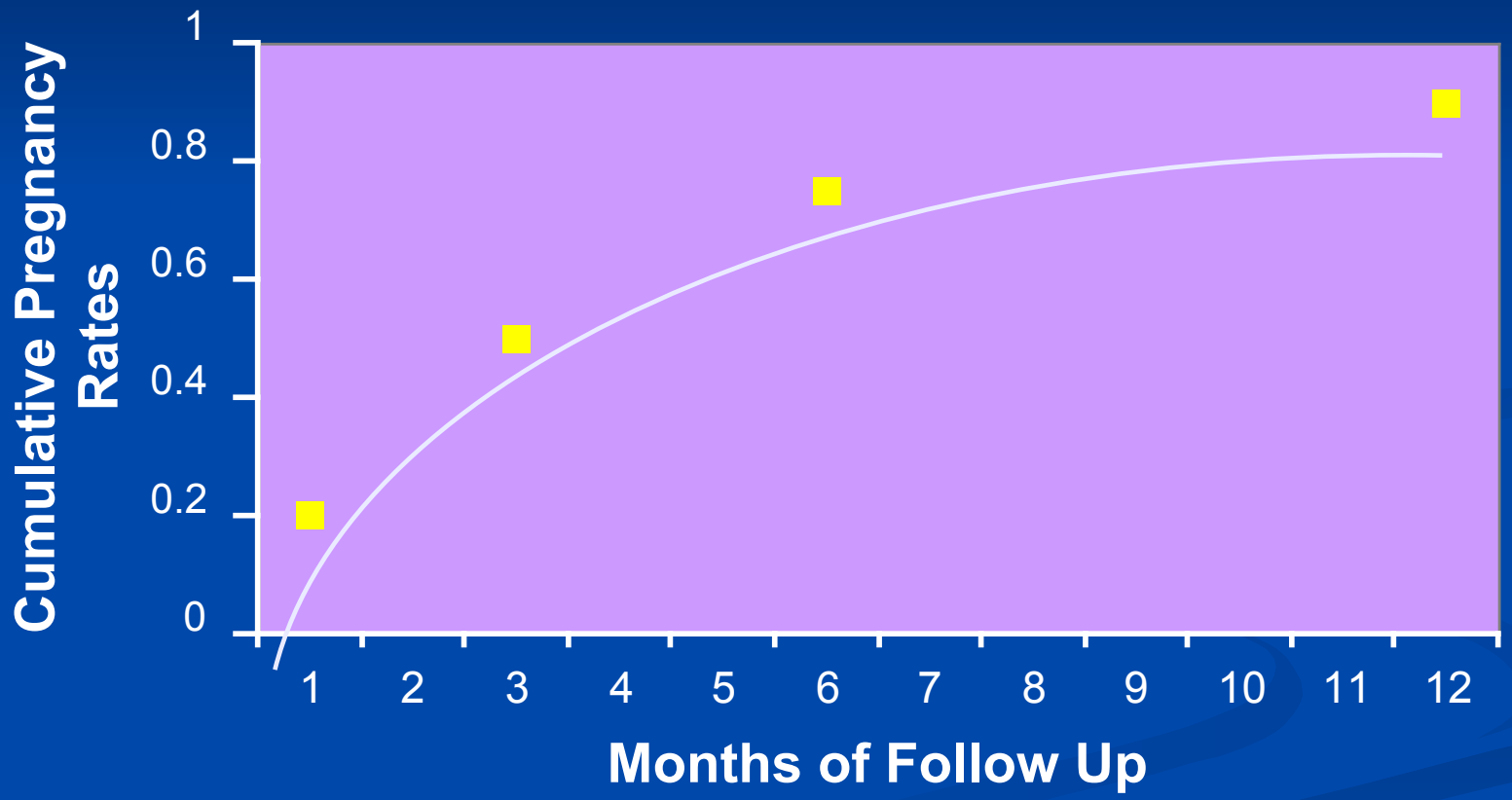
What percentage of the population is subfertile or infertile?

a. 1-2%
b. 5-10%
c. 10-15%
d. 15-20%
e. 20-25%

Outline

- Infertility
- Treatment Options
  - In Vitro Fertilization
  - Egg Freezing
  - Surrogacy
- Genetic Testing
  - Preconception
  - Preimplantation
  - Prenatal
- Controversies

Normal Fertility



Hull, et al: Br Med J 1985:291;1693

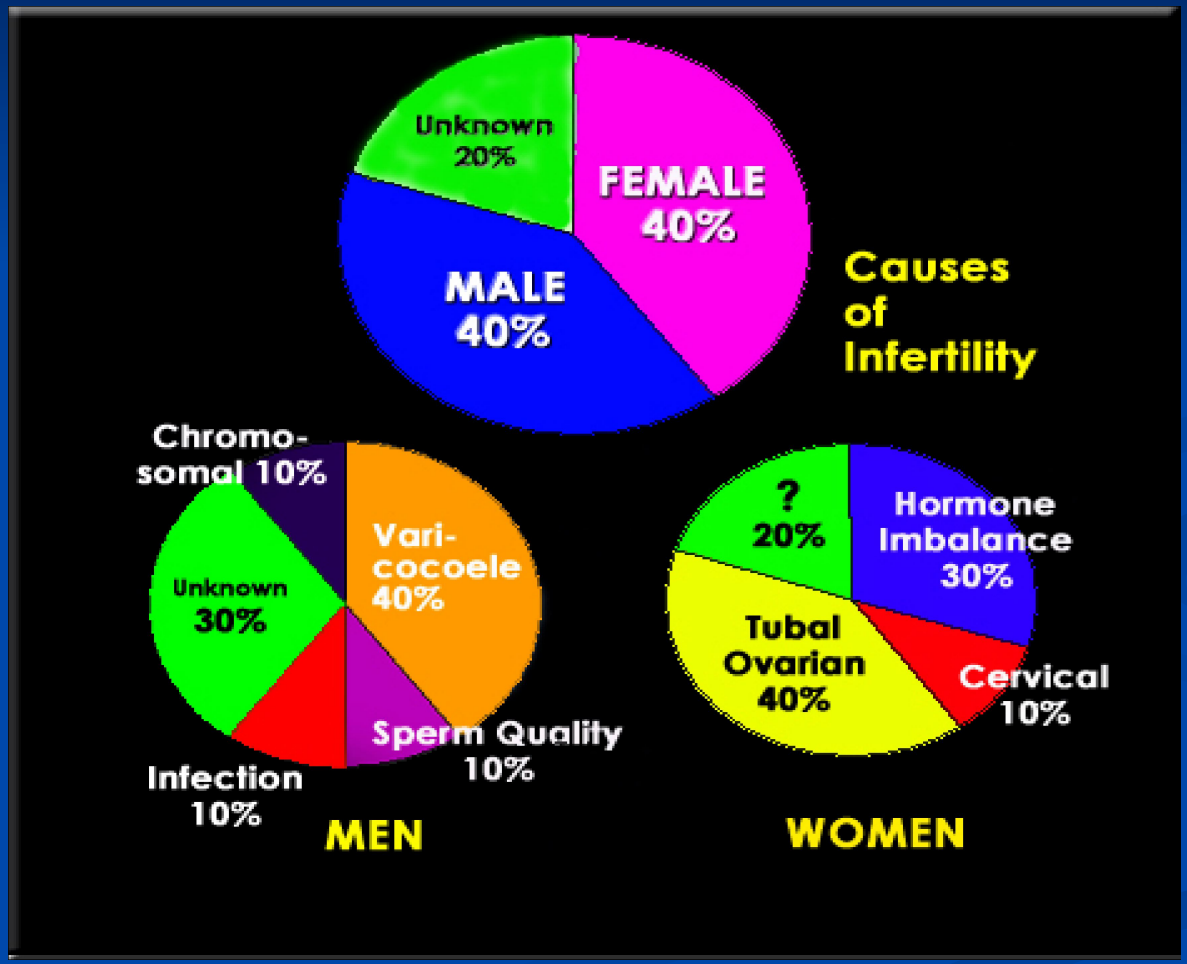
Overview of Infertility

- Definition: 1 year of well-timed, unprotected intercourse without a pregnancy
- 10-15% of population is infertile (subfertile)

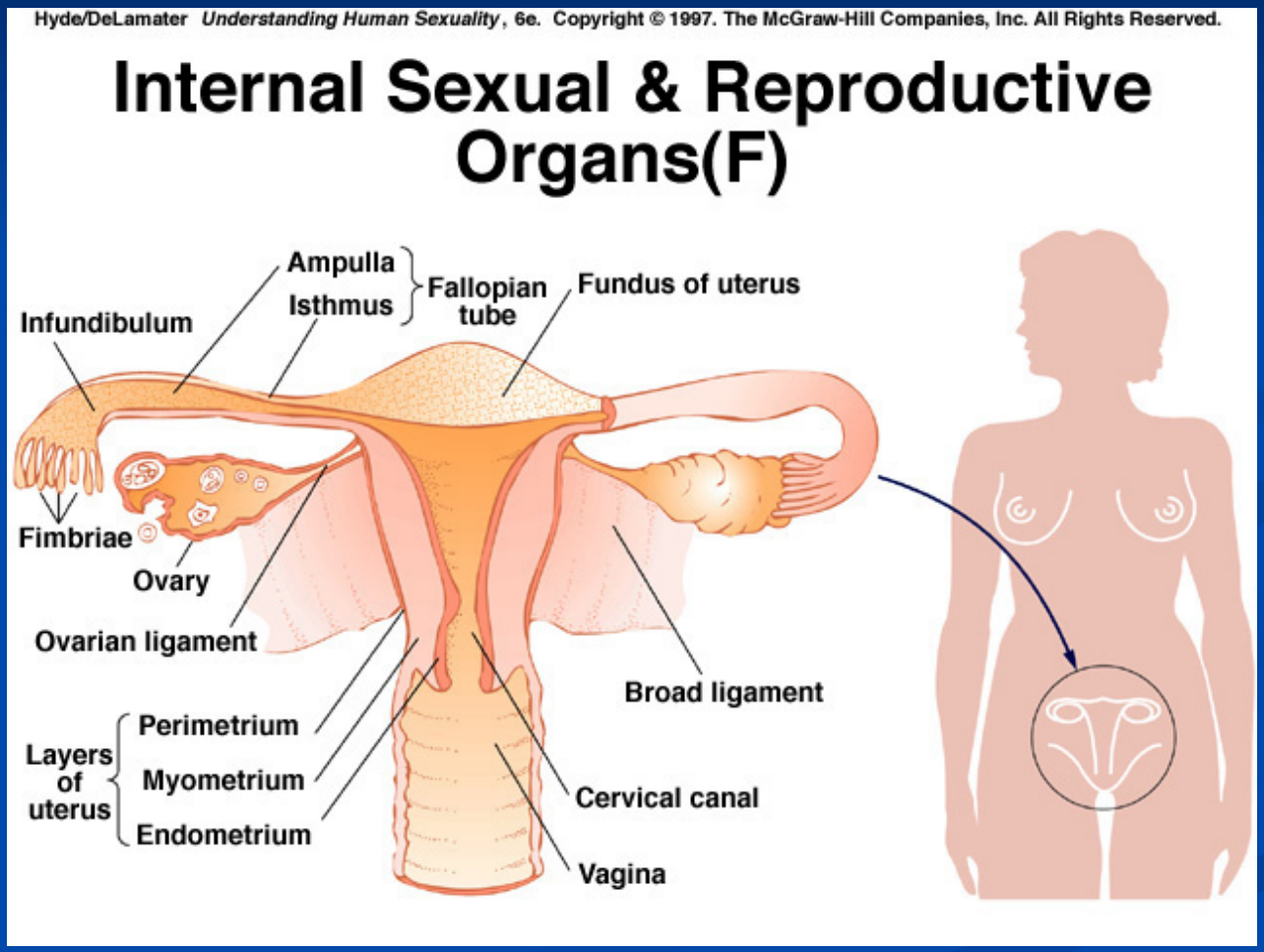
What factor might cause problems with fertility?

a. boxer shorts
b. drinking a glass of wine every day
c. eating disorder
d. hiking for 30 minutes per day
e. history of yeast infections

Causes of Infertility



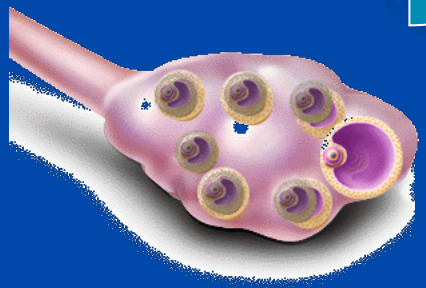
Female Reproductive Organs



Physiology

FSH
(+)

E2
(-)



Developing follicle

FSH=Follicle Stimulating Hormone

E2=Estradiol

Causes of Female Infertility

- Ovary
- Tubes
- Uterus
- Cervix
- Hormones
- Chromosomes

Causes of Female Infertility - Ovary

- AGE
- Problems with ovulation
- Premature ovarian failure

Do women continue to produce eggs throughout their life (from puberty until death)?

a. Yes
b. No

Ovary - Female Age

- Women are born with their lifetime egg supply
  - 4 million at 20 weeks gestation
  - 400,000 at birth
- 100,000 eggs left at time of puberty
- Fertility initially declines at age 27
- Significant decline at age 37-38
- Rare pregnancies after age 44

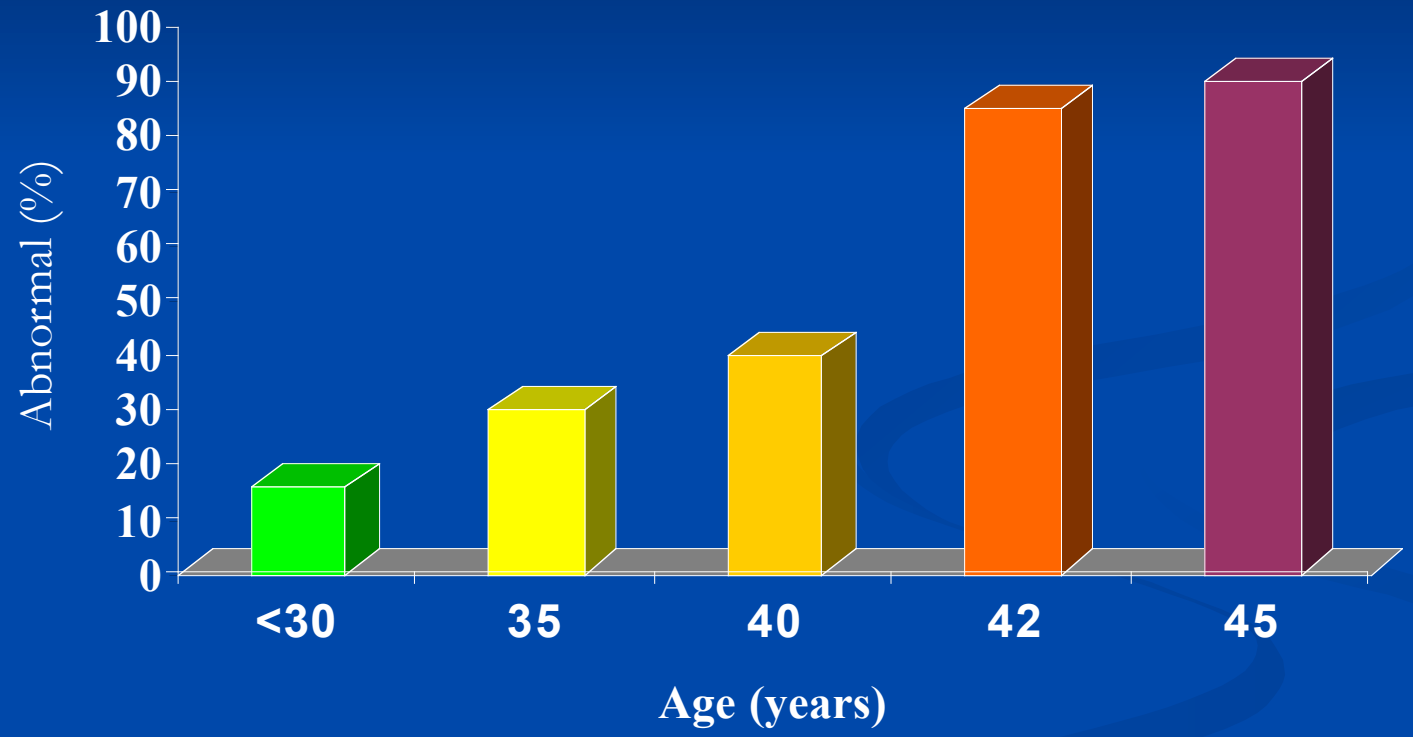
Percentage of Married Women Who are Infertile

From 3 national U.S. surveys

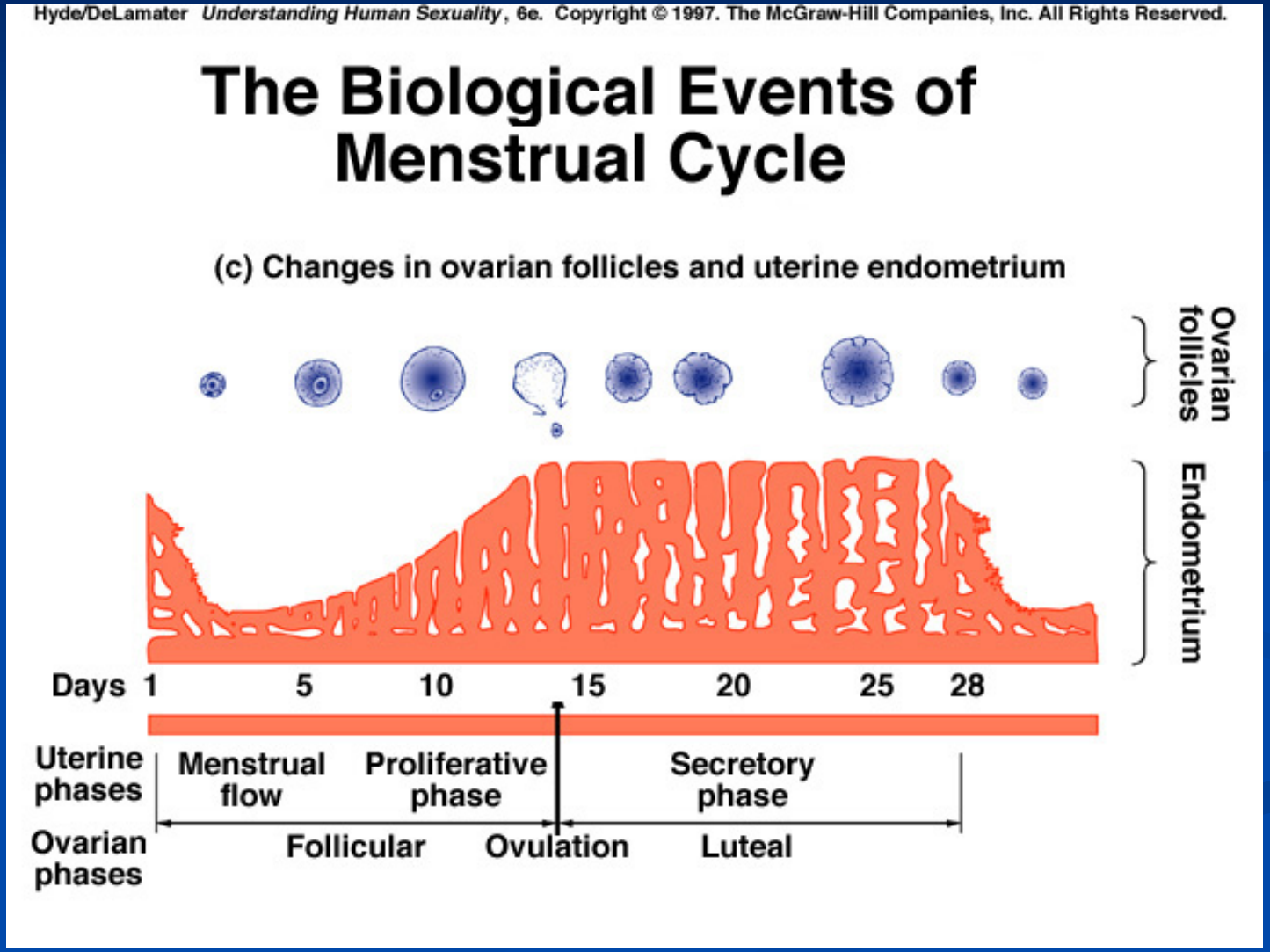
Age (years)	Infertile
20-24	7.0
25-29	8.9
30-34	14.6
35-39	21.9
40-44	28.7

Menken et al, Science 1989;23:1389

Prevalence of genetically abnormal oocytes in infertile women



Ovary - Ovulation



Ovary - Causes of Anovulation

- Hormone imbalance
- Obesity
- Anorexia
- Significant stress
- Patients display:
  - Irregular menstrual cycles
  - Skipped cycles
  - Minimal or absent premenstrual symptoms

Ovary – Premature Ovarian Failure

- Menopause prior to age 40
  - Decreased Estrogen
  - Increased FSH
- Causes
  - Autoimmune
  - Genetic
  - Idiopathic
- 1-2% pregnancy rate

What factor would not cause a woman's fallopian tubes to be blocked?

a. diabetes
b. ruptured appendix
c. endometriosis
d. chlamydia infection
e. tubal ligation

Causes of Female Infertility – Fallopian Tubes

- Infection (chlamydia)
- Endometriosis
- Tubal ligation (female sterilization)

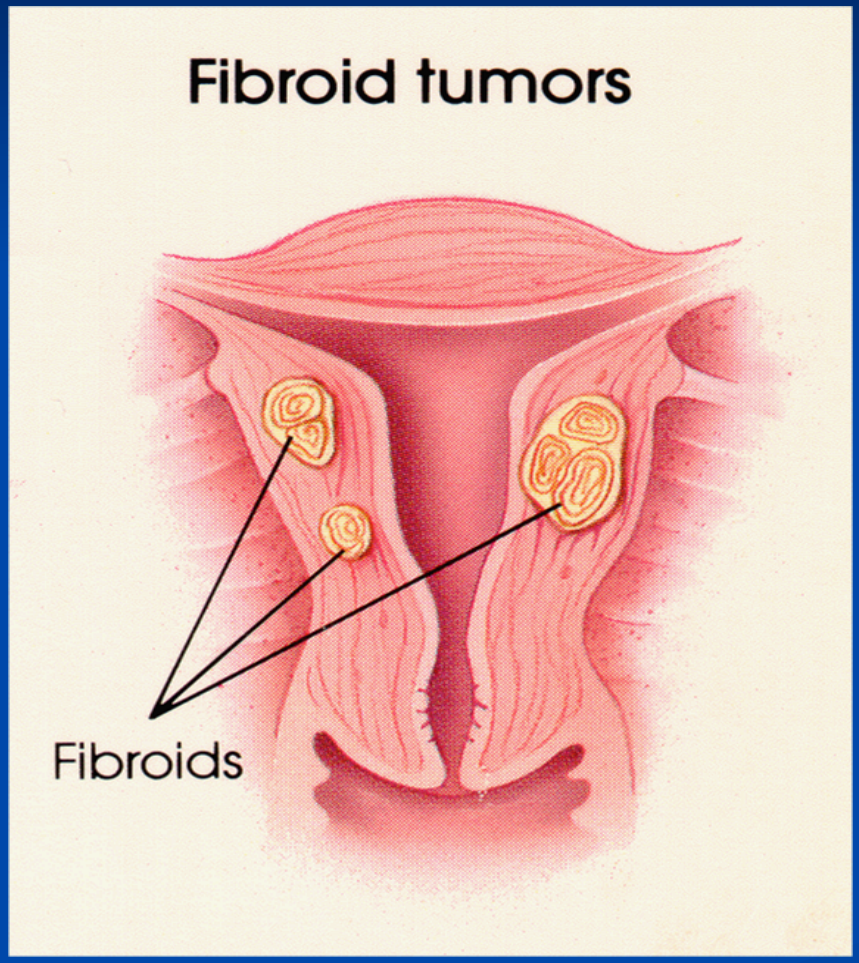
Open Tubes

Blocked Tubes

Female Infertility - Uterus

- **Uterus**
  - **Fibroids**
  - **Polyps**
- Mullerian (congenital) defects
  - Absent
  - Bicornuate/Septum

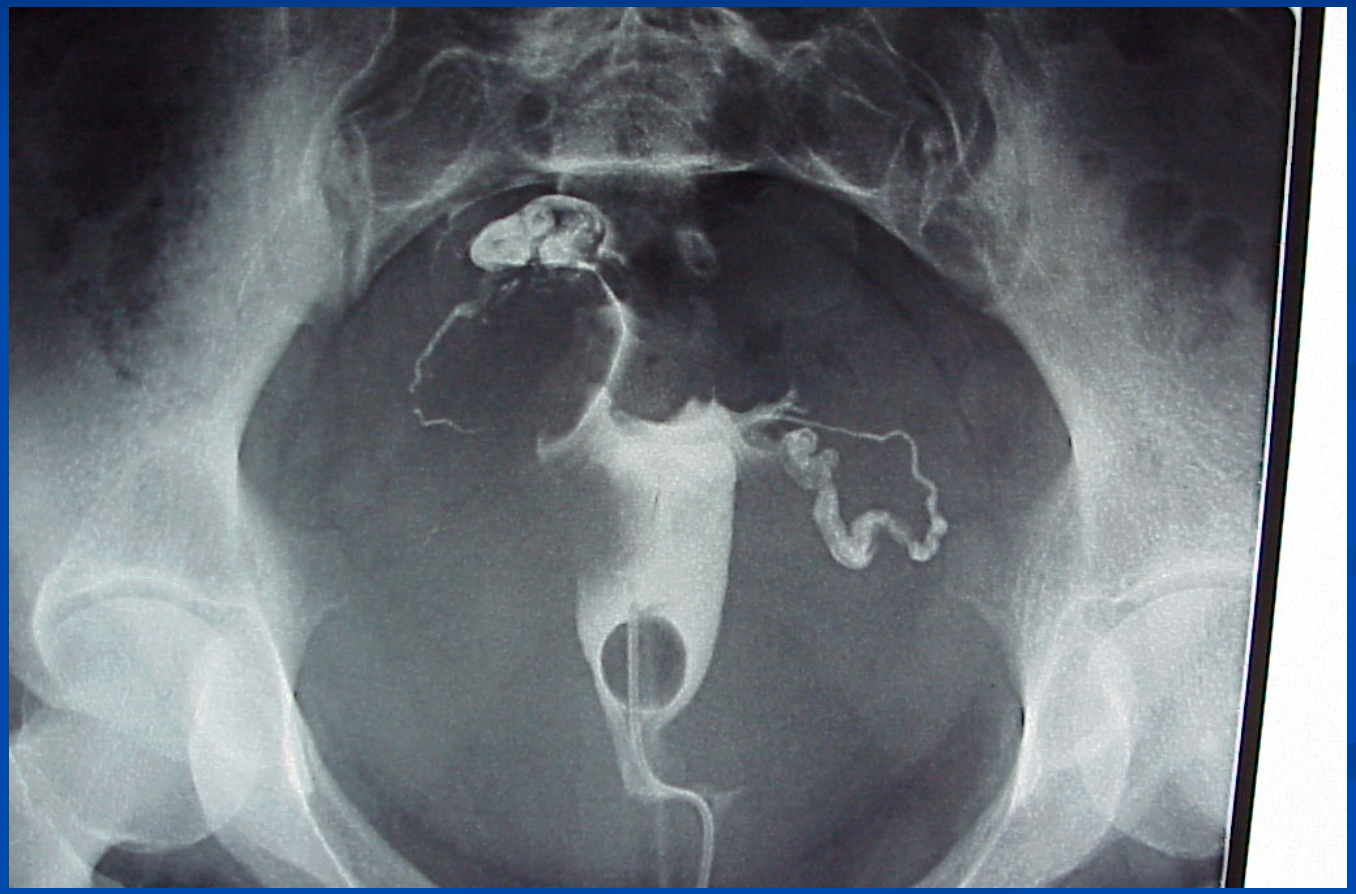
Female Infertility



- Uterine muscle tumor
- Benign (>95%)
- 25-30% of women

Normal Shape of Uterus

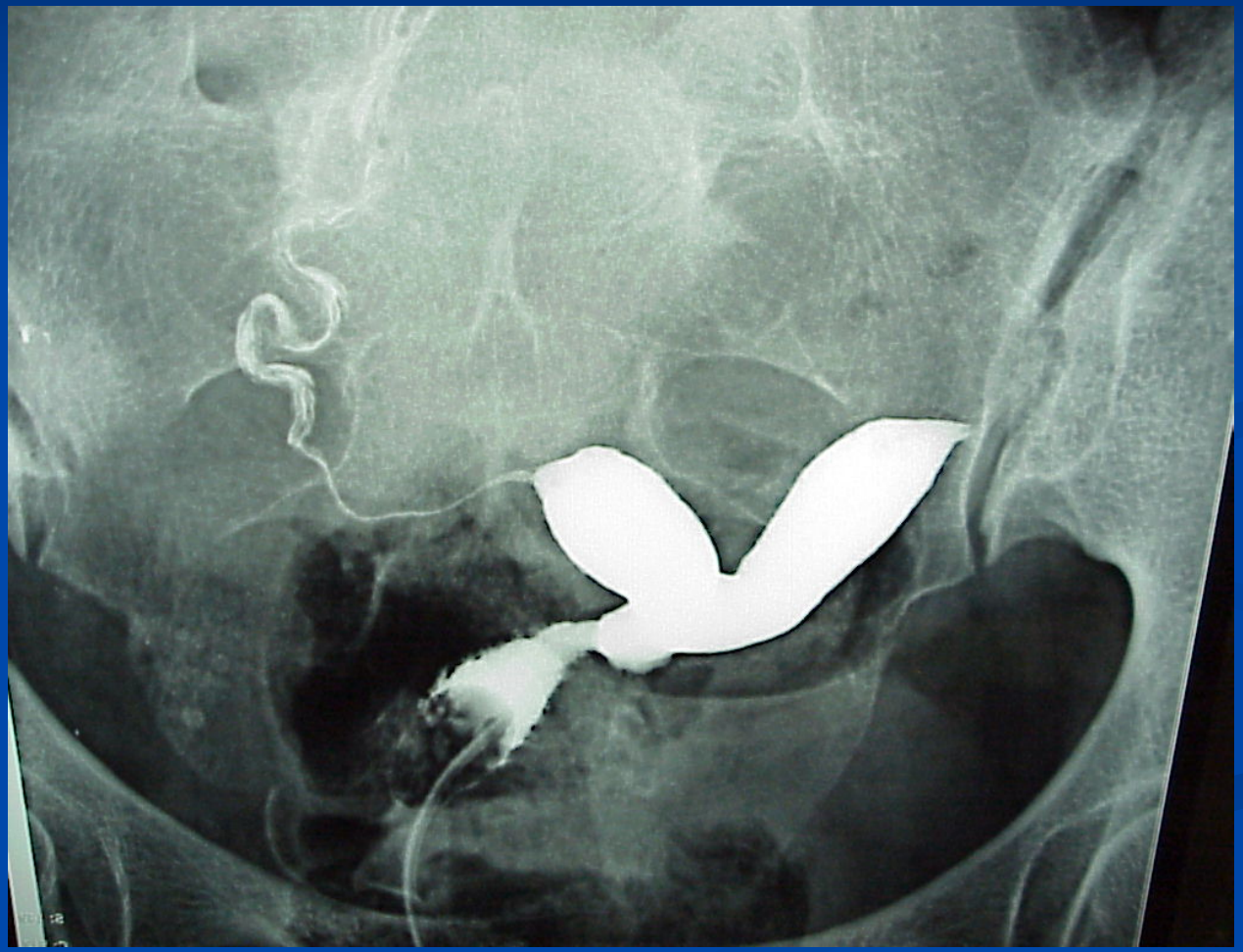
Fibroid Uterus



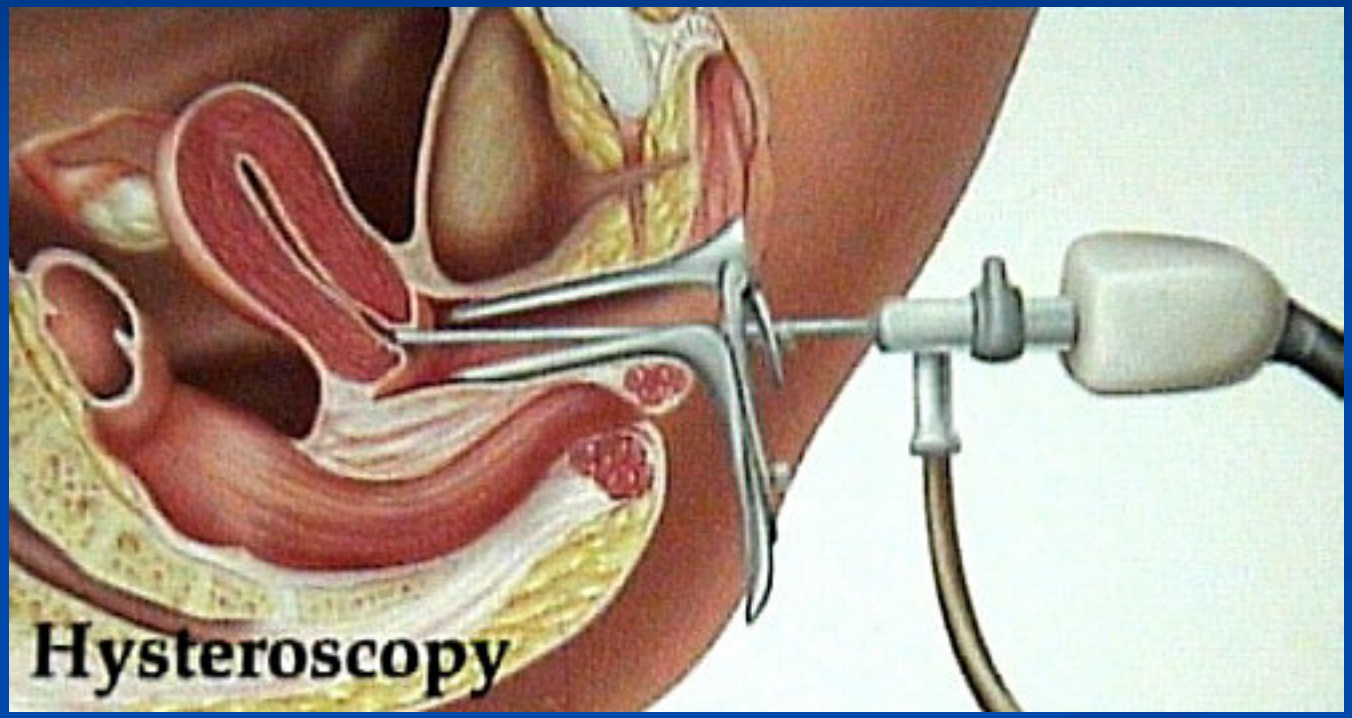
Female Infertility - Uterus

- Uterus
  - Tumors
    - Fibroids
    - Polyps
  - **Mullerian defects (congenital)**
    - **Absent uterus**
    - **Bicornuate/septate**

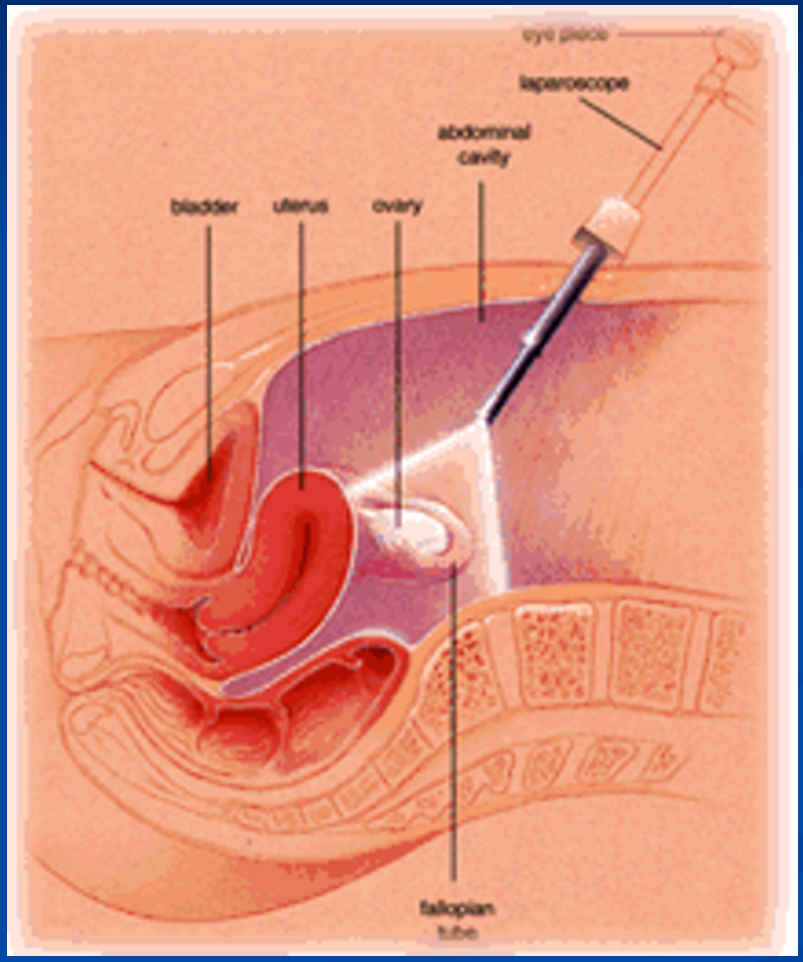
Mullerian Defect



Treatment with Hysteroscopy



Treatment with Laparoscopy



Surrogate Mothers, Inc.

Alternatives to Infertility since 1984.©

Female Infertility - Cervix

- Cervix
  - Post-surgical
    - Stenosis
    - Mucus changes

Female Infertility - Hormones

- Endocrine abnormality (hormones)
  - Thyroid
  - Prolactin
  - Polycystic ovary syndrome (PCOS)
    - Estrogen, insulin
  - Hypothalamic hypogonadism
    - Stress
    - Exercise (ballet dancer)

Other Causes of Female Infertility

- Others
  - Chromosome abnormalities
    - Turner's syndrome (XO)
    - Androgen Insensitivity (XY)
      - Male pseudohermaphrodite
      - Female phenotype
      - Blind vaginal canal
      - Inguinal hernia (50%)

Sperm Are Also Required!!

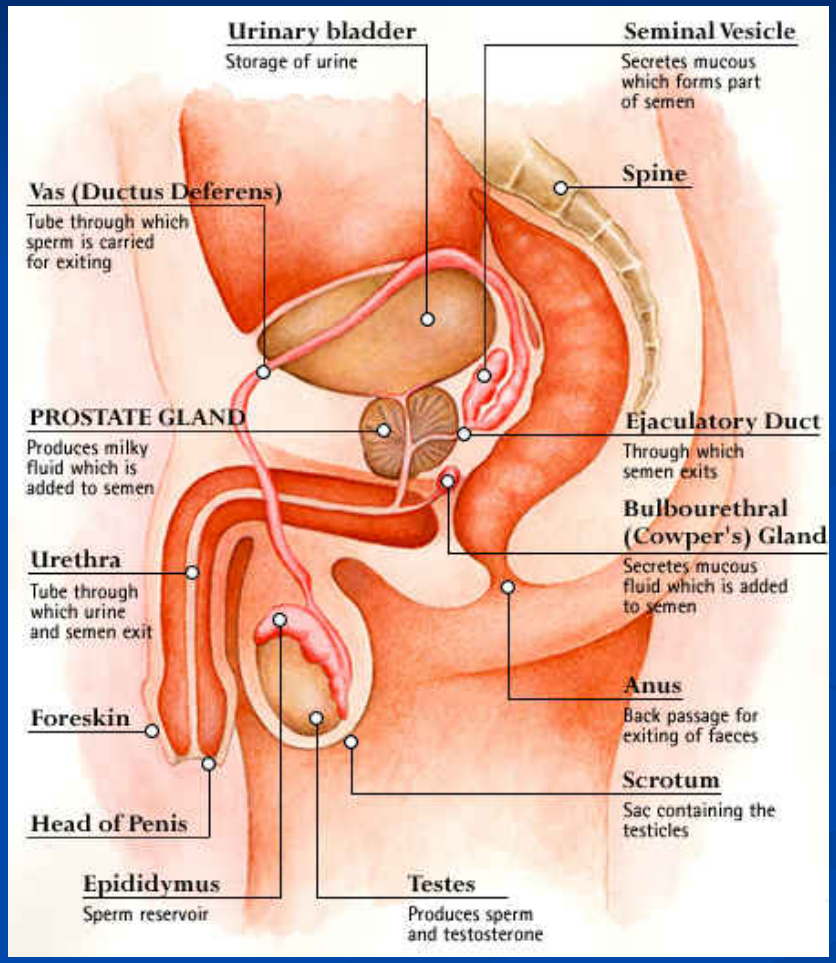
Do men continue to produce sperm throughout their life (from puberty until death)?

a. Yes
b. No

Causes of Male Infertility

- Abnormality in sperm production
- Abnormality in sperm function
- Obstruction in the ductal system

Male Reproductive Organs

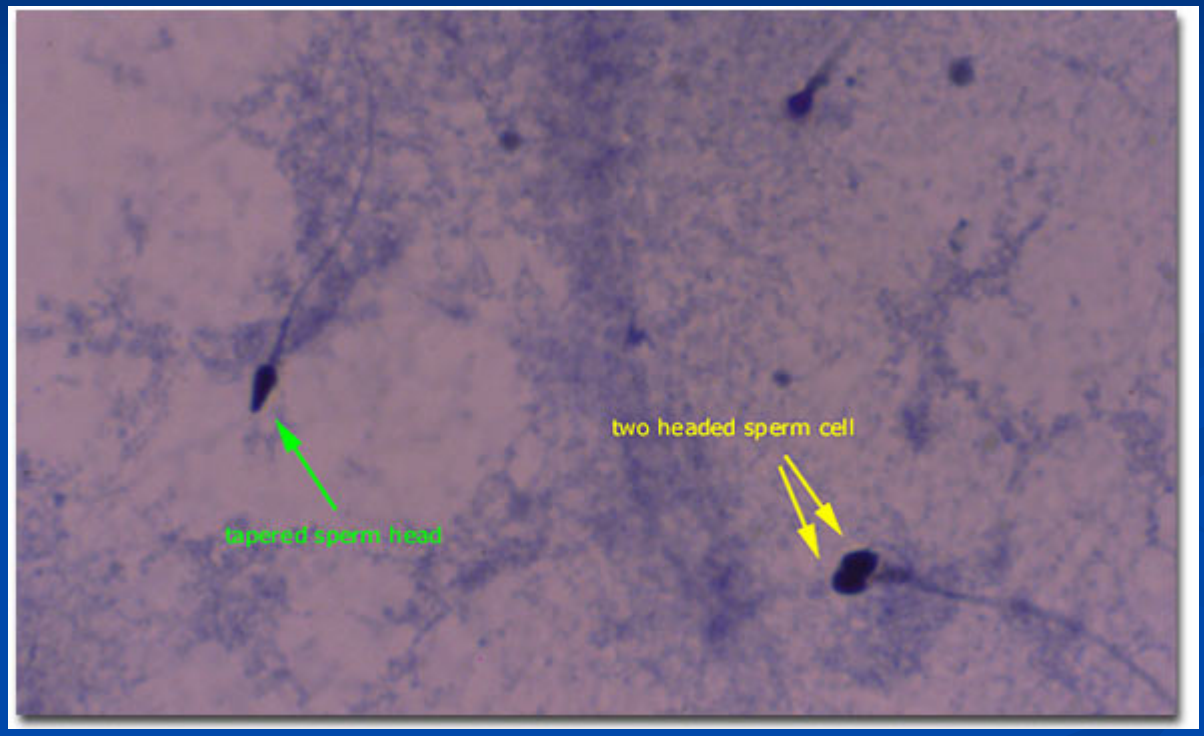


Sperm: Semen Analysis

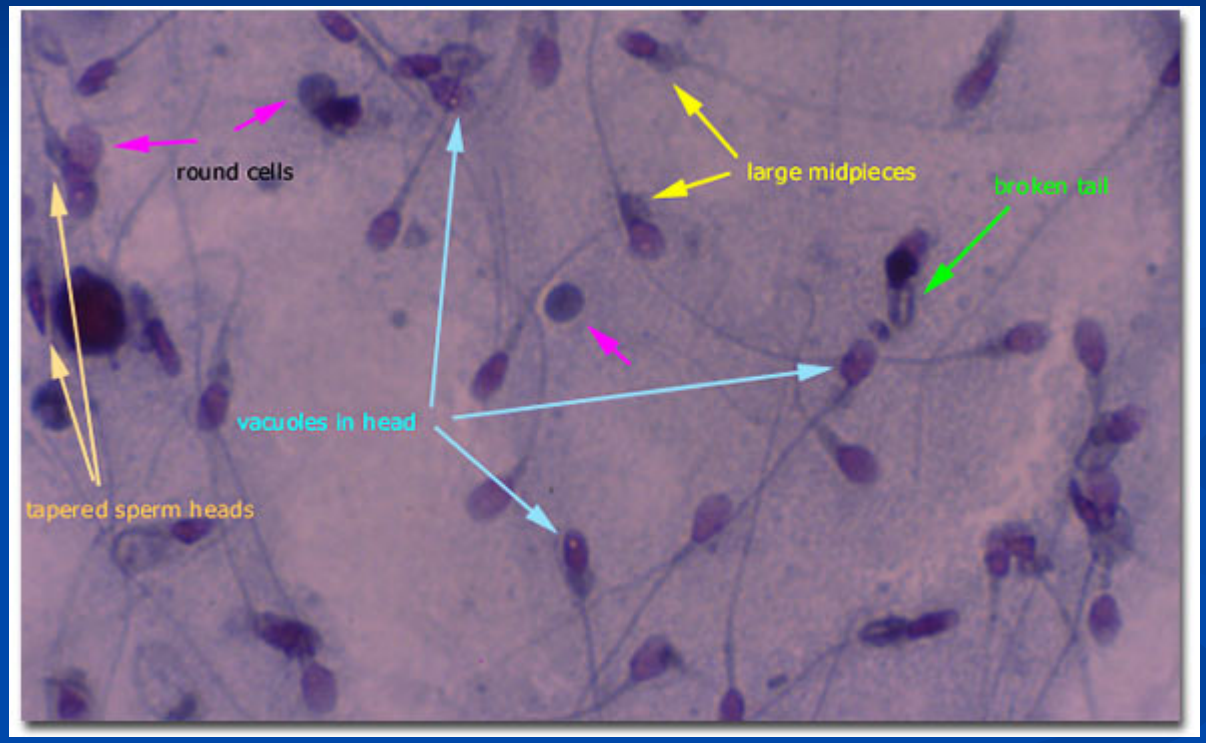
- Volume: $\geq$ 2 mL
- Concentration: $\geq$ 20,000,000 per mL
- Motility: $\geq$ 50%
- Normal morphology: $\geq$ 40% normal
  - Krueger strict criteria: $\geq$ 14% normal
  - Best predictor of fertilizing ability

Normal Sperm Morphology

Abnormal Morphology



Abnormal Morphology



Sperm

- **How many are needed for fertilization?**
- Natural conception
  - 20,000,000
- Intra-uterine insemination
  - 1,000,000
- In-vitro fertilization (IVF)
  - 10,000
- Intra-cytoplasmic sperm injection (ICSI)
  - 1

Causes of Male Infertility

- Abnormality in sperm production
- Abnormality in sperm function
- Obstruction in the ductal system

Abnormalities of Sperm Production

- Genetic
  - Y chromosome microdeletions
- Damage to testes – anatomical
  - Cryptorchidism
  - Varicocele
- Infection
  - Mumps orchitis
- Gonadotoxins

Abnormalities of Sperm Function

- Antisperm antibodies
- Genital tract inflammation
  - prostatitis
- Varicocele
- Failure of acrosome reaction
- Problems with sperm binding/penetration

Obstructions in Ductal System

- Vasectomy
- Congenital bilateral absence of the vas deferens
- Epididymis/ejaculatory ducts
  - Congenital or acquired

What percentage of men desire another pregnancy after having a vasectomy?

a. 1%
b. 5%
c. 10%
d. 25%
e. 100%

Male Infertility - Lifestyle

- Tobacco
- Marijuana
- Alcohol
- Cocaine
- Steroids (can be permanent)
- Heat
- Exercise

Infertility: Initial Evaluation

- Eggs
  - Ovulation
  - Egg quality
- Sperm
  - Presence
  - Quality
- Gamete transport/Implantation
  - Hysterosalpingogram

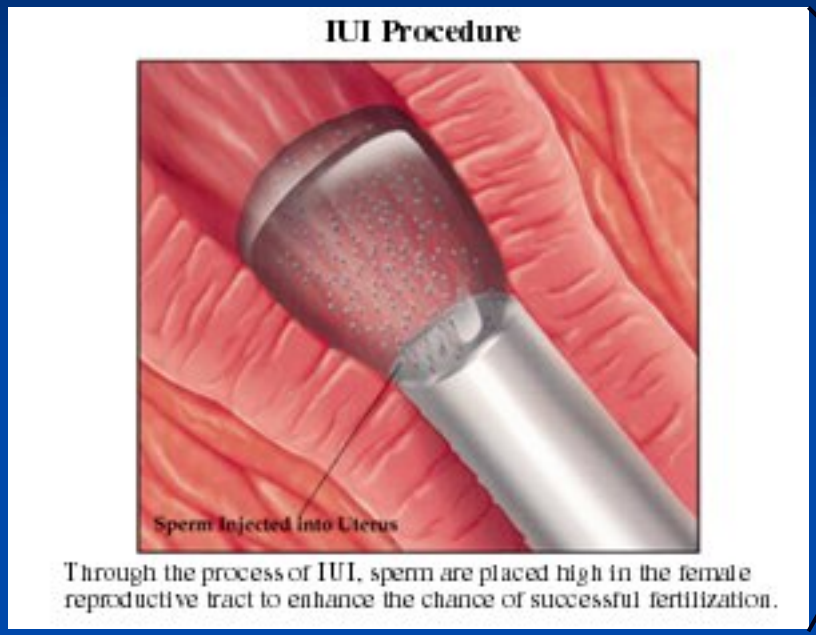
Unexplained Infertility

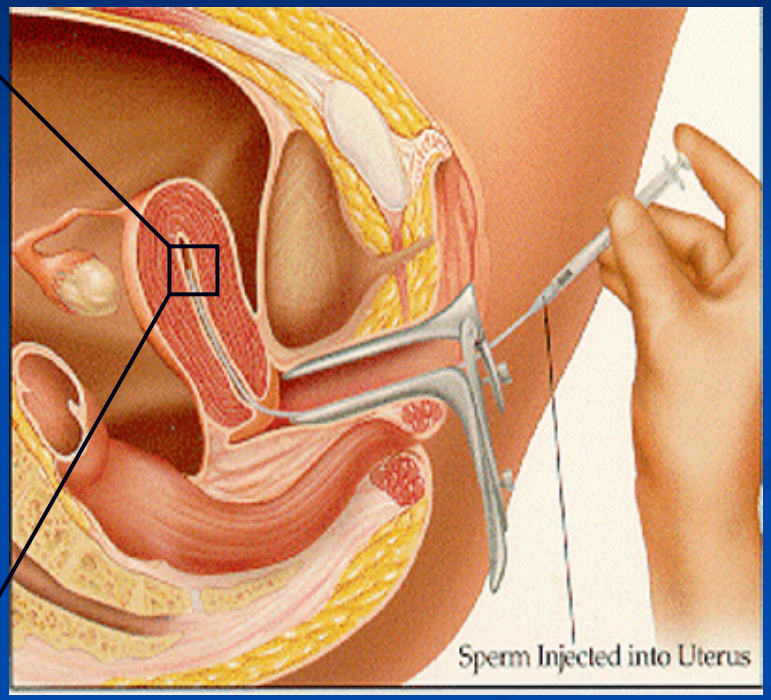
- Work-up is negative
- 15-20 % of couples

Infertility Treatments

- Improve Timing of Intercourse
- Intrauterine insemination (IUI)
  - Clomiphene citrate + IUI
  - FSH + IUI
- In Vitro Fertilization (IVF)
  - "Standard" IVF
  - Egg donation + IVF
  - Egg Freezing + IVF

Intrauterine Insemination (IUI)





Goal is to Maximize the Chance of Fertilization

- **Increase Number of Eggs**
- **Position Sperm Closer to Eggs**

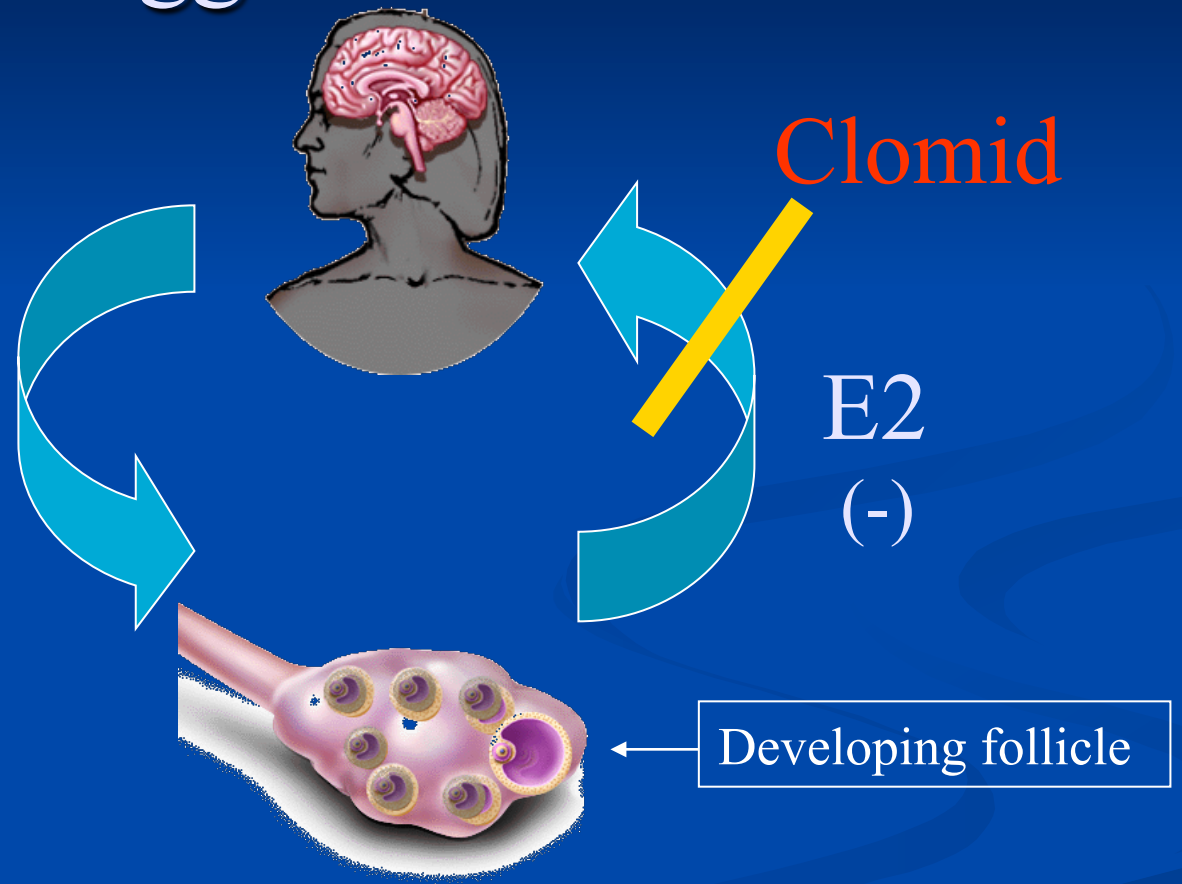
Infertility Treatment Options

- IUI, FSH or FSH + IUI
- Patients with unexplained infertility

Treatment	Cycles	Pregnancy	Pregnancy per cycle
IUI	30	1	2.7%
FSH	49	3	6.1%
FSH+IUI	34	9	26.4%

Serhall et al, Fertil Steril 1988;49:602

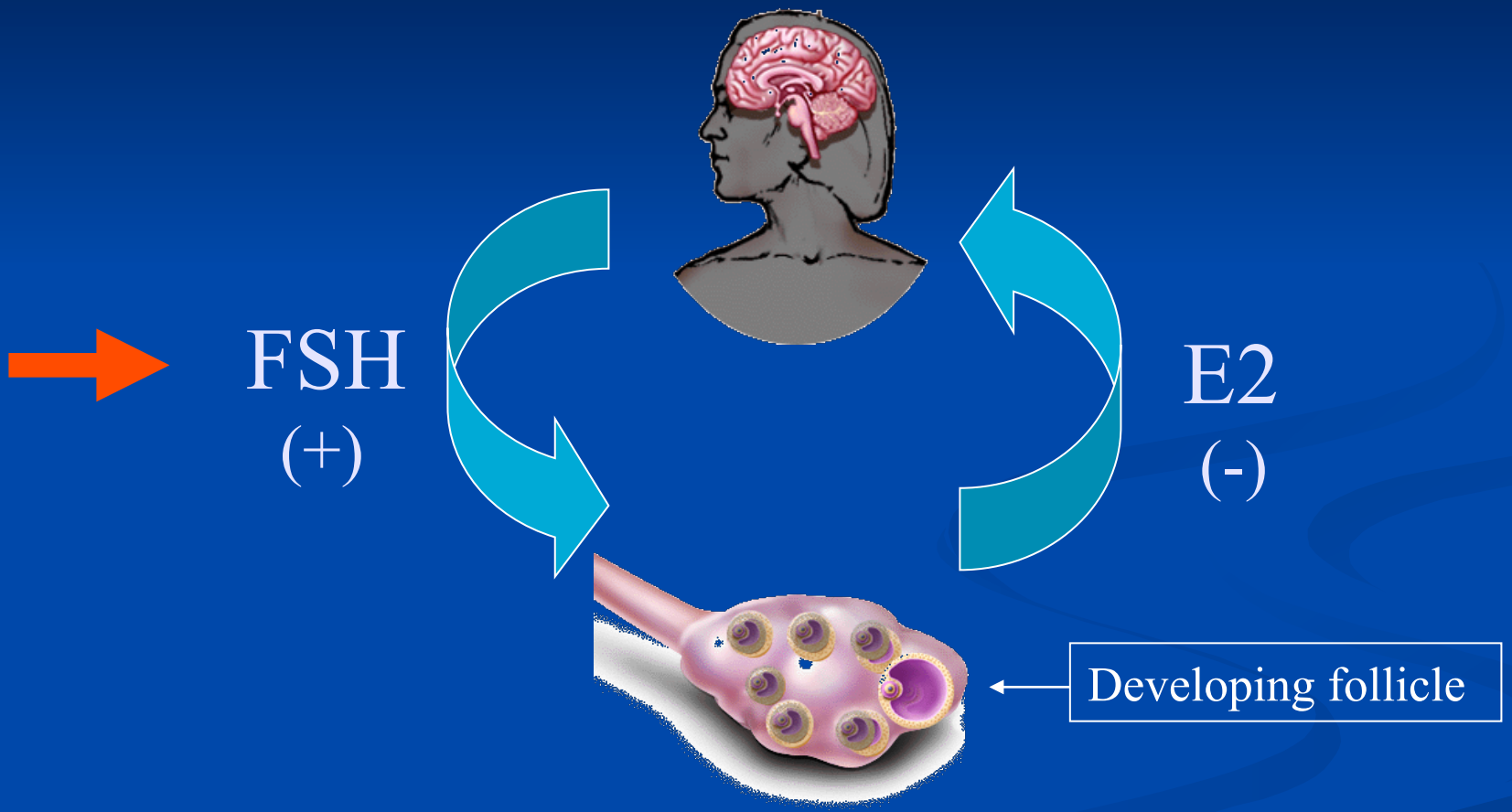
How Does Clomid Work To Increase Egg Number?



FSH=Follicle Stimulating Hormone

E2=Estradiol

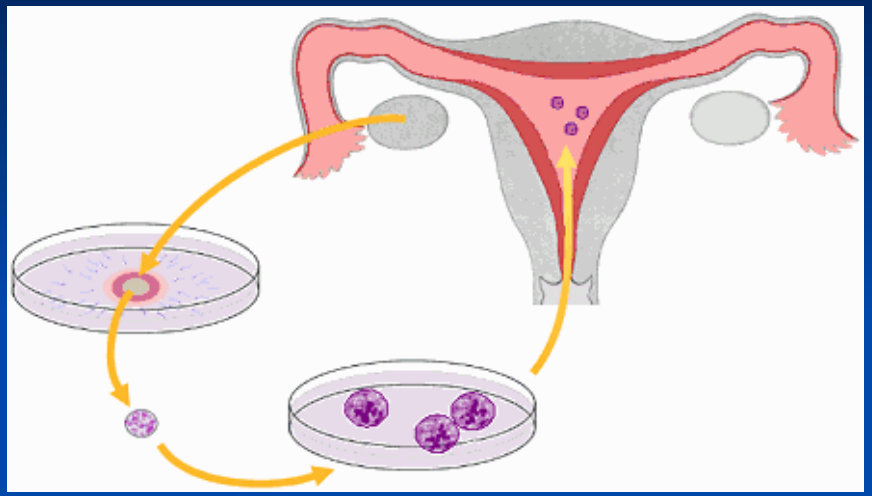
How Does Recombinant FSH Work To Increase Egg Number?



FSH=Follicle Stimulating Hormone

E2=Estradiol

In Vitro Fertilization



Why In Vitro Fertilization?

- Infertility
- DNA Testing
  - Genetic Disorders
  - Gender Selection
- Non-Traditional Life Styles

Who should decide if a couple/person can have infertility treatment?

a. state governments
b. national fertility agencies (ASRM)
c. reproductive specialists
d. psychologists/psychiatrists
e. the couple/person

Should a 52 year old postmenopausal woman be able to use her daughter's eggs to have a child with her new 28 year old husband?

a. Yes

b. No

Should a woman be able to have sperm extracted from her husband's newly dead body so that she can have "their child"?

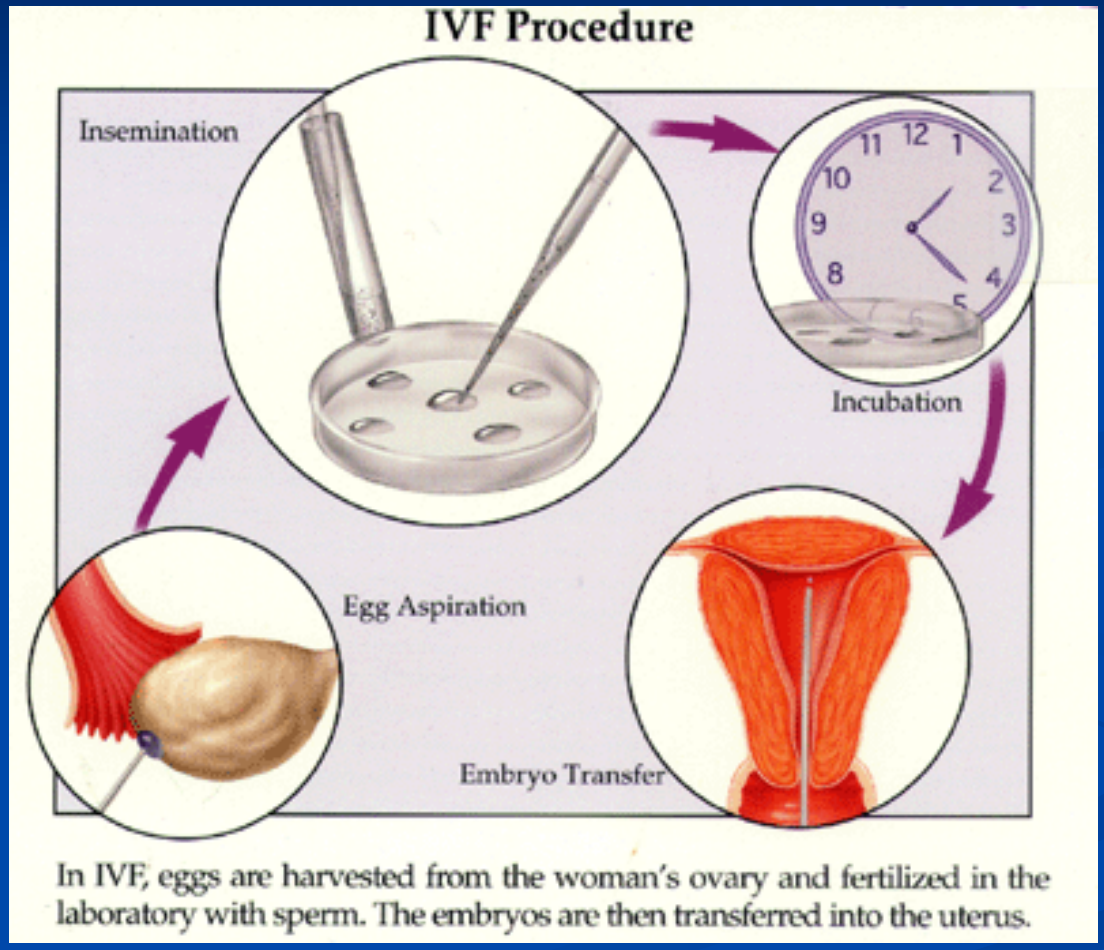
a. Yes

b. No

In Vitro Fertilization - History

- 1978 – First "test tube" baby was born in England
- 1981 – IVF in U.S.
- Started with GIFT and ZIFT
- 2008 - >98% IVF with transfer of embryo to uterus

In Vitro Fertilization (IVF)



In IVF, eggs are harvested from the woman's ovary and fertilized in the laboratory with sperm. The embryos are then transferred into the uterus.

IVF Statistics - 2005

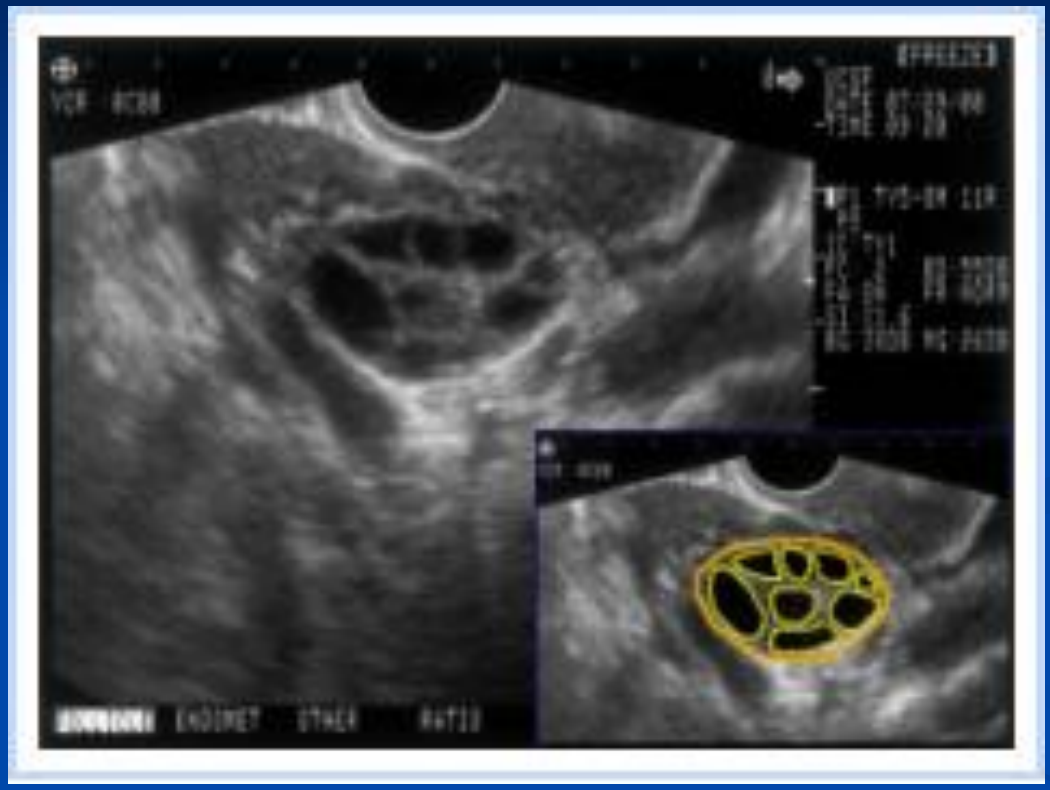
- 422 U.S. programs offer IVF
- 134,260 cycles of ART treatment
- 9,649 donor oocyte cycles
- 38,910 deliveries (birth of 52,041 neonates)

CDC 2005 National Report

Who Needs IVF?

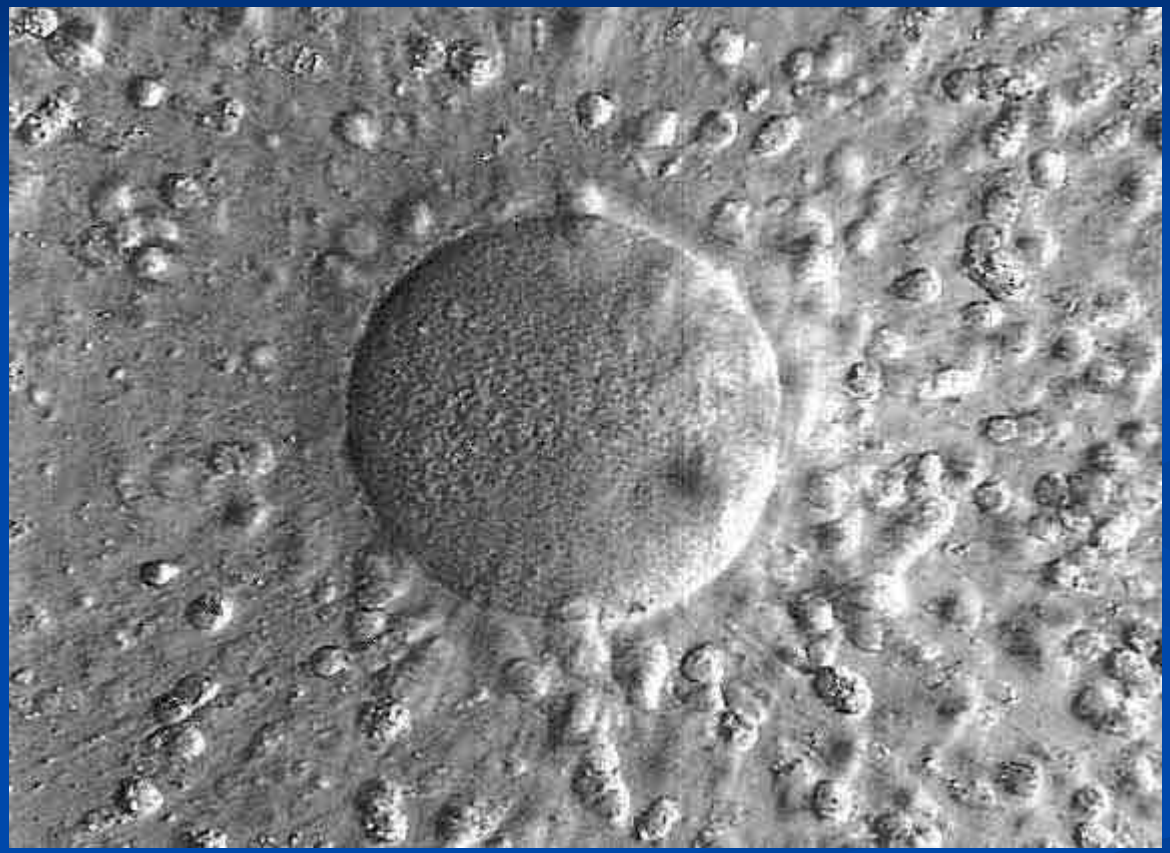
- Failed other treatments
- Tubal damage
- Significant male factor
- Absent uterus
- Carriers of genetic diseases
- Gender selection
- Cancer patients
- Non-traditional lifestyle

Ovarian Hyperstimulation

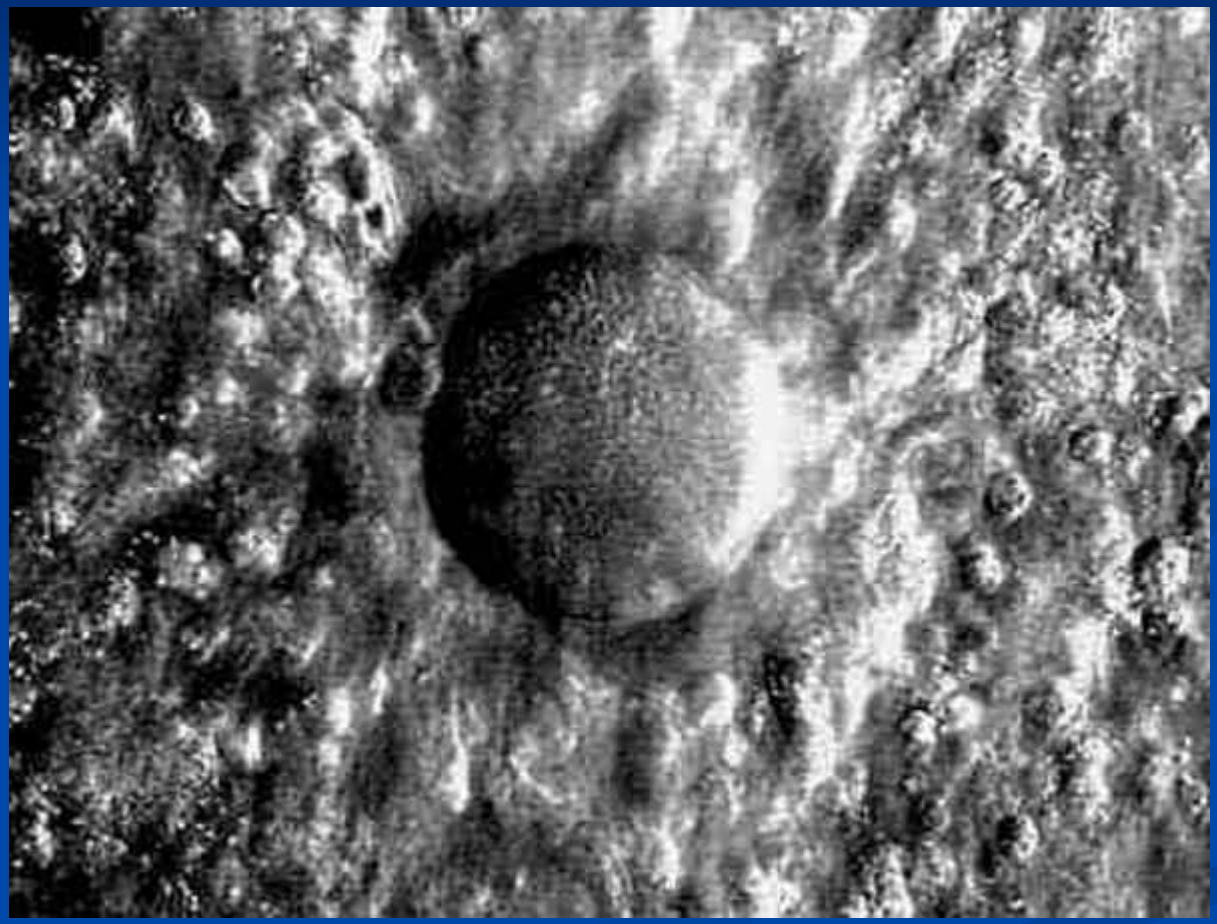


Egg Retrieval

Good Egg



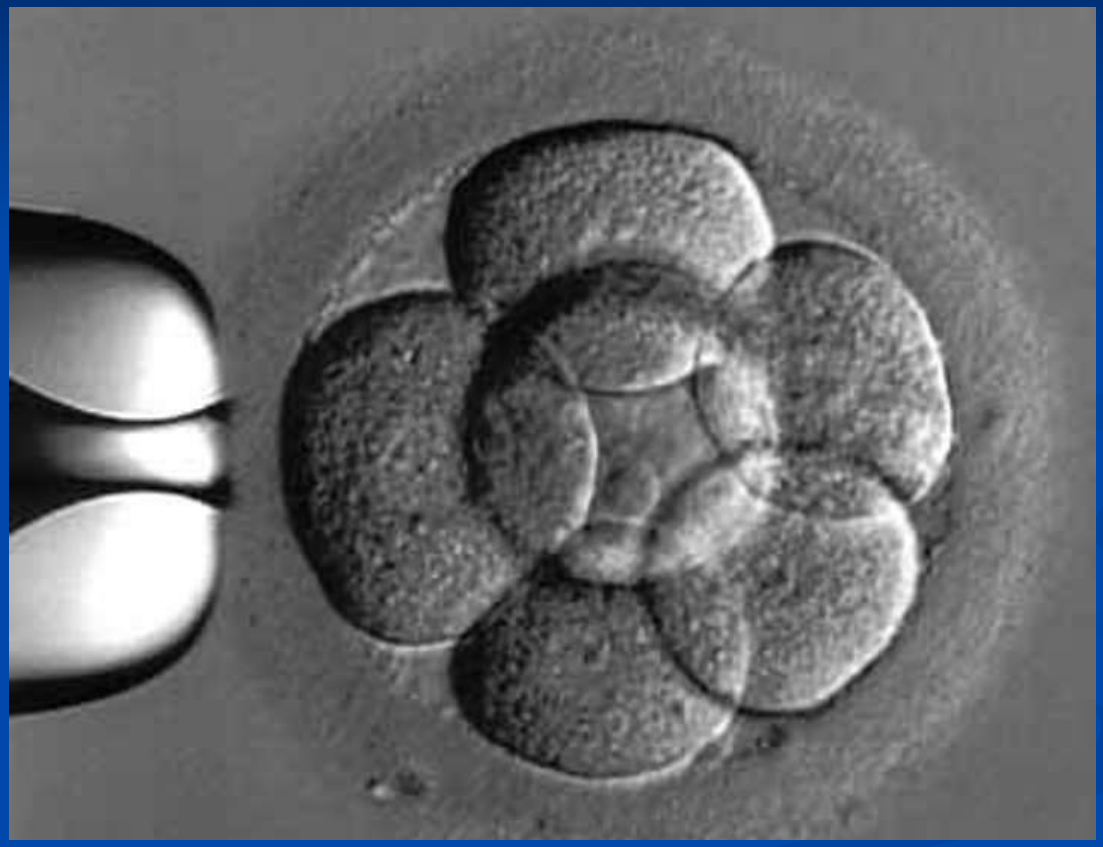
Bad Egg



Fertilization

- 2 Pronuclei (2PN)
- 1 day after egg retrieval

Day 3 Embryo



Pre-Implantation Genetic Testing Stage

Day 3 Embryo

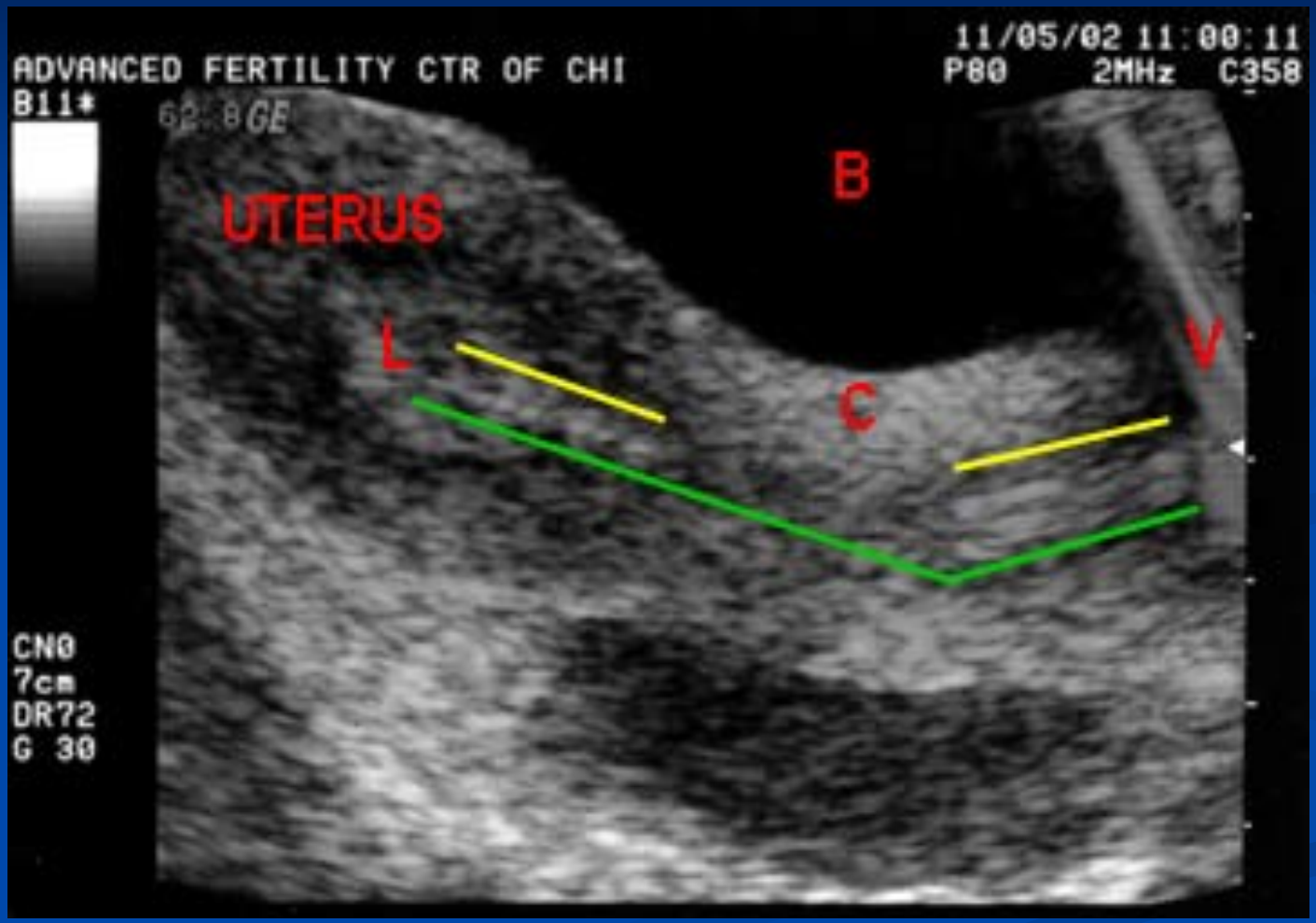
Blastocyst – Day 5

Source of Stem Cells

Hatching Blastocyst

Embryo Transfer

Embryo Transfer



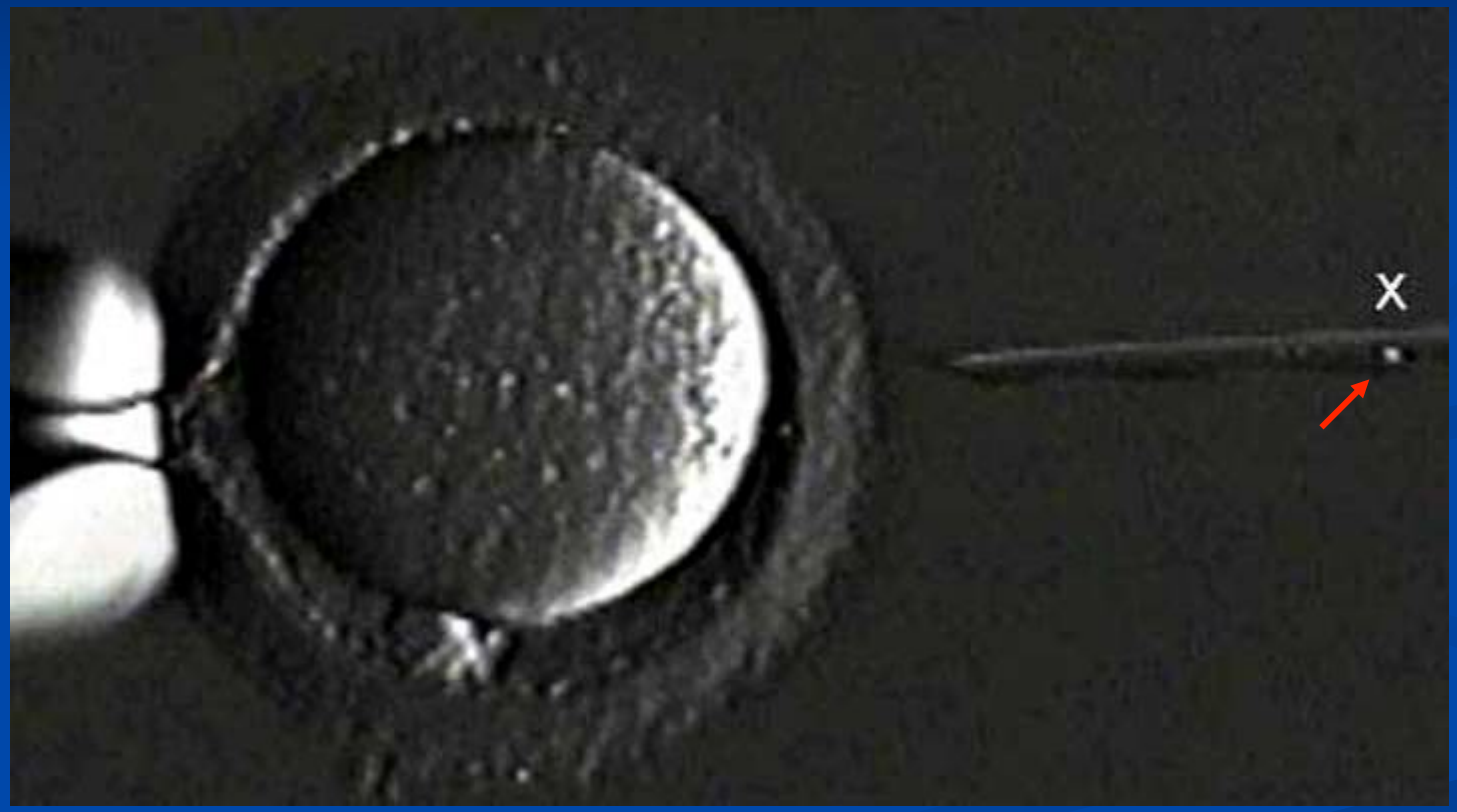
Special IVF Procedures

- Assisted hatching
- Intracytoplasmic sperm injection (ICSI)
- Preimplantation genetic diagnosis (PGD)
- Freezing
- Egg donation
- Surrogacy

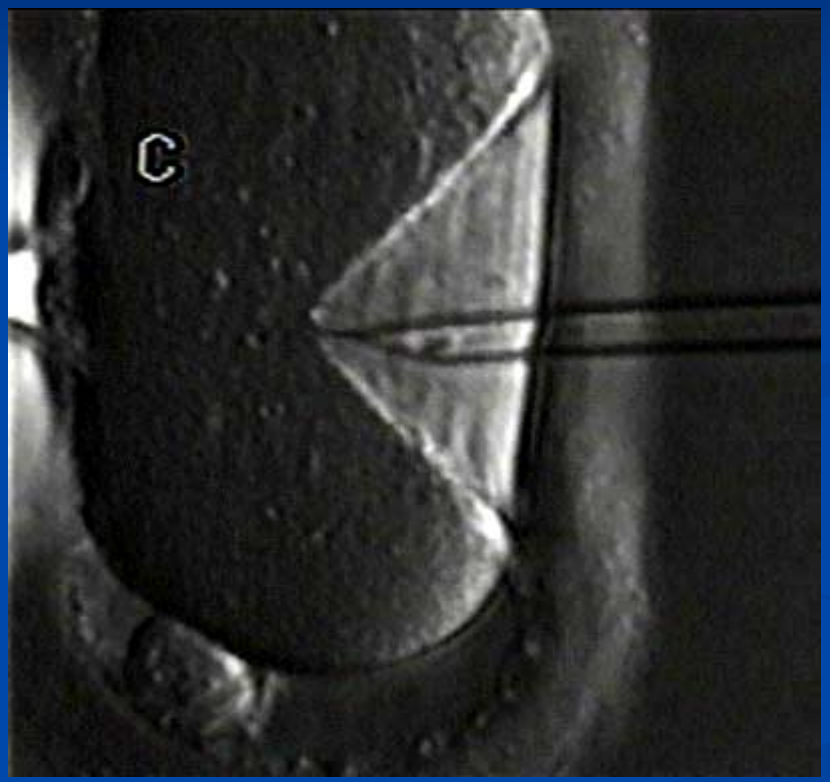
Assisted Hatching

Empty Zona

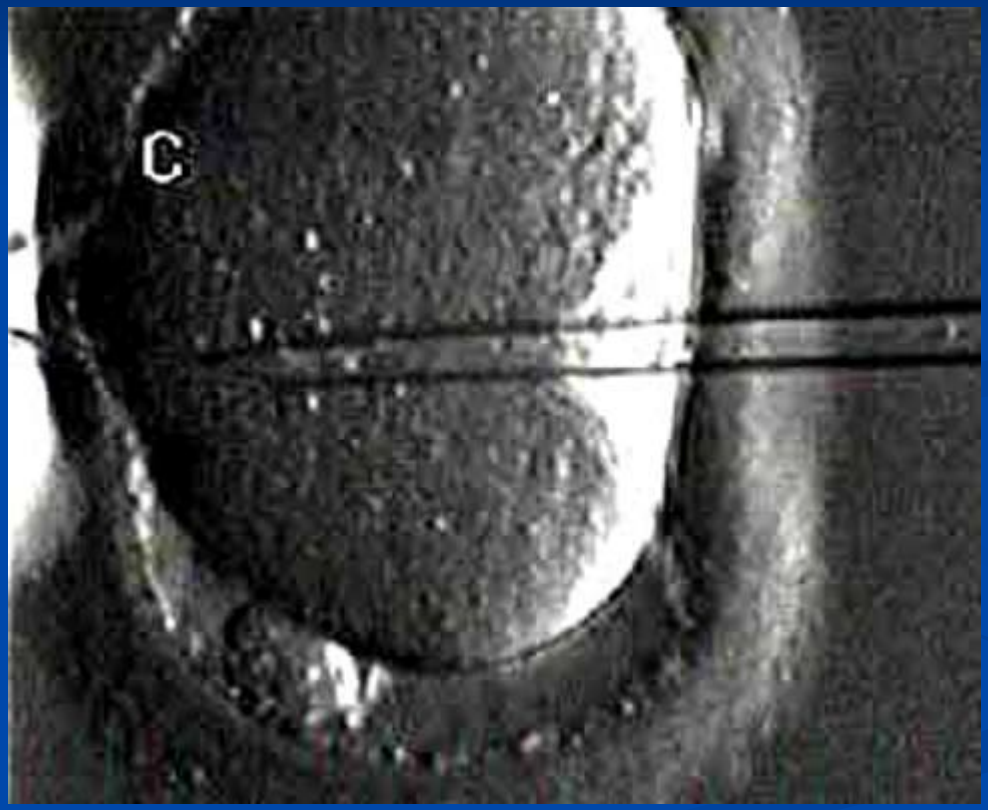
ICSI



ICSI



ICSI



What are the risks of IVF?

a. bleeding requiring blood transfusion
b. pelvic infection
c. increased risk of congenital anomalies
d. multiple pregnancies
e. all of the above

How many embryos are recommended to transfer into a 42 year old woman's uterus?

a. 1
b. 2
c. 3
d. 4
e. 5

How Many Embryos are Transferred?

- Related to age and embryo quality
  - <35 = 2
  - 35-37 = 2-3
  - 38-40 = 3-4
  - >40 = up to 5

  - For patients with 2 or more failed IVF cycles, or a poor prognosis, can add more based on clinical judgement

What Happens to the Other Embryos?

- Freeze Embryos
- Donate For Research/Stem Cells
- Embryo Adoption
- Discard

What Would You Do With Your Embryos?

a. Freeze and Store Them
b. Donate For Research (e.g., Stem Cells)
c. Donate To Others For Adoption
d. Discard

IVF Success Rates - 2005

- U.S. Fertility Centers From SART/CDC (HRC)
- Female age
  - <35 – 37% (43%)
  - 35-37 – 30% (36%)
  - 38-40 – 20% (27%)
  - >40 – 11% (18%)

IVF Statistics - 2000

- 65.1% singletons (16,533)
- 30.8% twins (7,817)
- 3.9% triplets (1,000)
- 0.2% higher order multiples (44)

Singleton Pregnancy

Twin Pregnancy

Triplet Pregnancy

IVF and Multiple Pregnancy

- Maternal complications
- Fetal complications
- Cost
- "Selective reduction"
- Single embryo transfer vs. success rates

Cost of IVF

- IVF cycle + medications = $10,000-15,000
- Assisted hatching = $500
- ICSI = $1,500
- Freezing = $650
- Storage = $360
- Egg Donor = Minimum $5,000
- Surrogate = Minimum $10,000-15,000

Not Covered By Insurance In Most States!

Egg Donation

EXCEPTIONAL DONORS

Exceptional Donors, Inc. was founded to help couples struggling with the pain of infertility in the Portland, Oregon area and throughout the United States. Egg donation is a wonderful way for families to grow. And we can help. Allow us to assist you as you begin your journey toward becoming a parent.

We are always searching for exceptional donors. If you are between 19 and 32 years of age, healthy, intelligent, athletic, artistic, musically talented, attractive, or possess other exceptional qualities, you could be a candidate for our program.

We offer $5,000 compensation for first-time donors, and more for subsequent donations.

Call 866.296.1015 or visit www.exceptionaldonors.com to learn more about becoming an exceptional egg donor.

Would you consider being an egg or sperm donor?

a. Yes

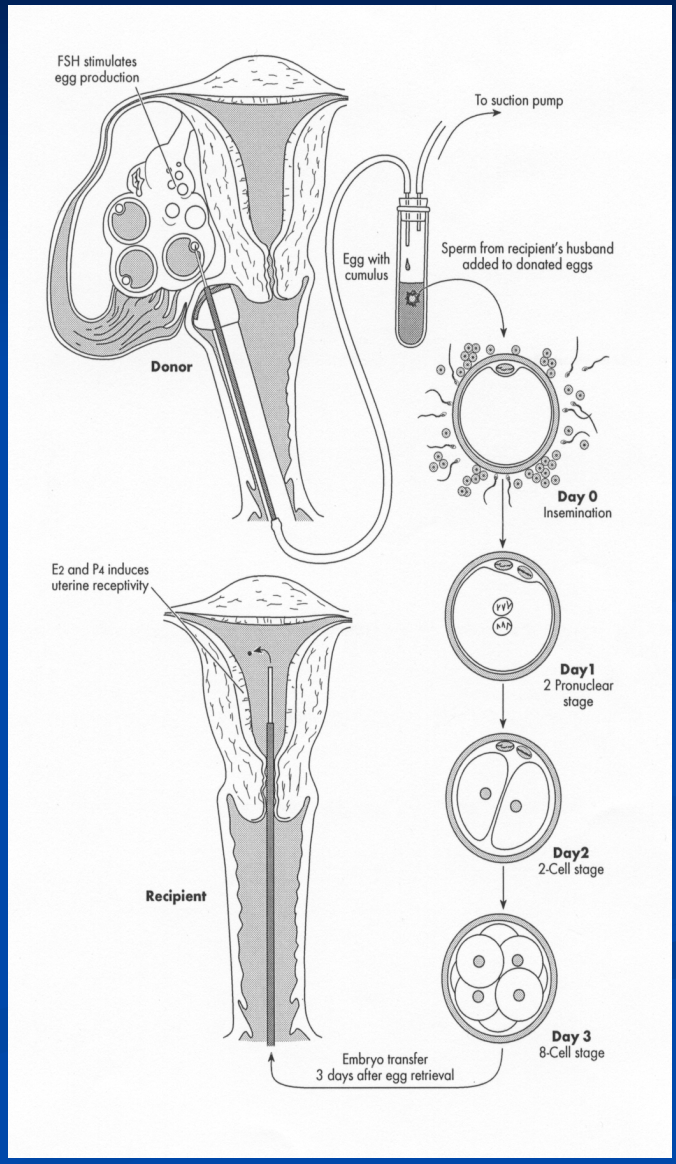
b. No

Have you ever been an egg or sperm donor?

a. Yes
b. No

Egg donation

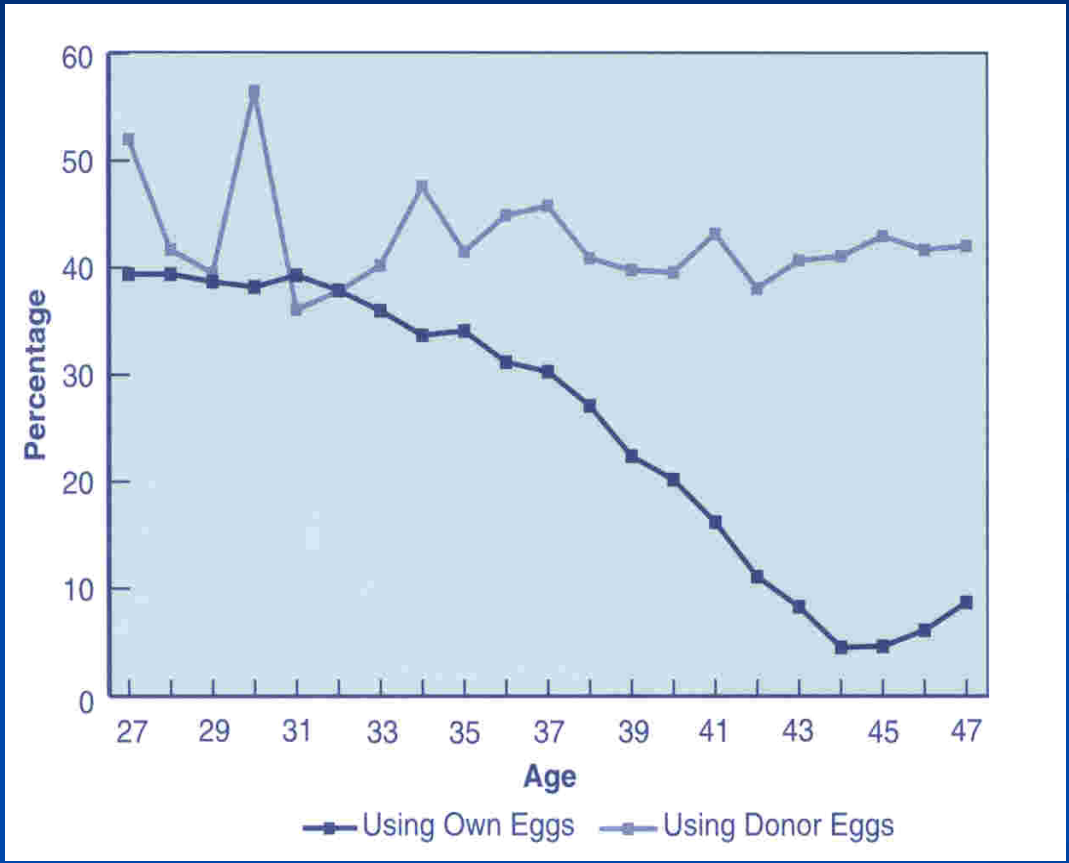
- IVF for two
- Donor
  - Standard controlled ovarian hyperstimulation
  - Egg retrieval
- Recipient
  - Embryo transfer



Who are candidates to be an egg donor ?

- 21-35 years old (older if a friend or relative)
- FSH <10
- Negative donor
- Good health and genetic history
- Preferably prior egg donation experience
  - How many eggs were produced?
  - Did pregnancy result?

Current status of ART in the USA



Live birth rates
per transfer
for fresh embryos
from own and
donor eggs,
by age of recipient

SART registry, 1998

Egg Donation

Grade A: The Market for a Yale Woman's Eggs

When a Yale undergraduate explored becoming an egg donor for a wealthy couple willing to pay top dollar to the right candidate, she didn't realize how unsettling the process of candidacy would prove to be

by Jessica Cohen

Egg Donation

- October 23, 1999
- Selling Fashion Models' Eggs Online Raises Ethics Issues
- By CAREY GOLDBERG

- CAMBRIDGE, Mass. -- To the horror and disgust of mainstream infertility groups, a longtime fashion photographer has begun offering up models as egg donors to the highest bidders, auctioning their ova via the Internet to would-be parents willing to pay up to $150,000 in hopes of having a beautiful child.

Egg Donation - Ethical Issues

- Egg Donor
  - Known or anonymous
  - How many times to donate?
- Recipient
  - How old is too old?

Pregnancy in the Sixth Decade of Life

- USC experience: 1991-2000
  - 77 recipients of egg donation
  - Mean age 52.8 + 2.9 years
- Of the 77 women, 42 (54.5%) had live births
- 45 deliveries in 42 women

Paulson, Tourgeman, Boostanfar et al, JAMA 2002:228;2320.

Pregnancy in the Sixth Decade of Life: Obstetric Complications

- Pre-eclampsia
  - 35%
- Background Incidence
  - 3-10%
- Gestational Diabetes
  - 20%
- Background Incidence
  - 5%

How old is too old?

- Is 55 a "physiological limit"?
  - Marked increase in pre-eclampsia
  - Increase in diabetes

Genetic Testing

- Preconception
- Preimplantation
- Prenatal
- Postnatal

Preconception Counseling

- Offered to all women
  - Prenatal vitamins – 400 micrograms folic acid/day
  - Rubella immunity
  - Varicella immunity
  - Rh status
  - HIV
  - Hepatitis B screen
  - Cystic Fibrosis screening
  - Spinal muscular atrophy (SMA)

Preconception Counseling

- Offered to certain ethnic groups
  - Mediterranean – thalassemia
  - African-American – sickle-cell anemia
  - Caucasian/Hispanic – cystic fibrosis
  - Ashkenazi Jews – 7 autosomal recessive disorders
    - Gaucher disease (1/13), Tay-Sachs (1/30), Familial dysautonomia (1/30), Canavan disease (1/40), Fanconi anemia (1/89), Niemann-Pick disease (1/90), Bloom syndrome (1/100)

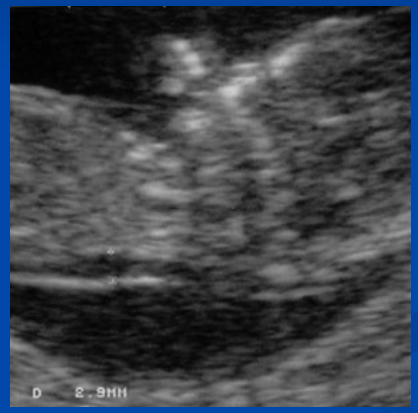
Prenatal Testing

- Ultrasounds
- Serum screens
- Chorionic villus sampling (CVS)
- Amniocentesis

Prenatal Tests - Ultrasound

- Nuchal translucency screening
  - Performed between 10-13 weeks gestation
  - Screen for Down Syndrome

Nuchal Translucency

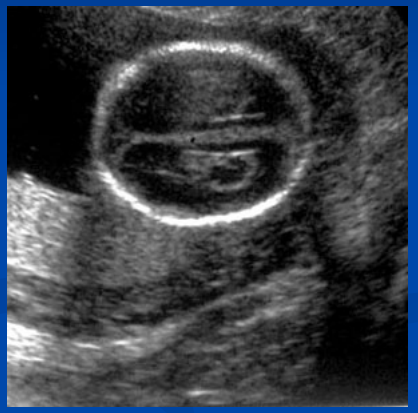


Prenatal Tests - Ultrasound

- Second trimester ultrasound
  - Detailed exam
  - Down Syndrome, other trisomies
  - Cardiac, renal, spinal, limb, brain deformities
  - Cleft lip/palate

Ultrasound Abnormalities

Echogenic bowerls



Ultrasound Abnormalities

Prenatal Tests - Serum

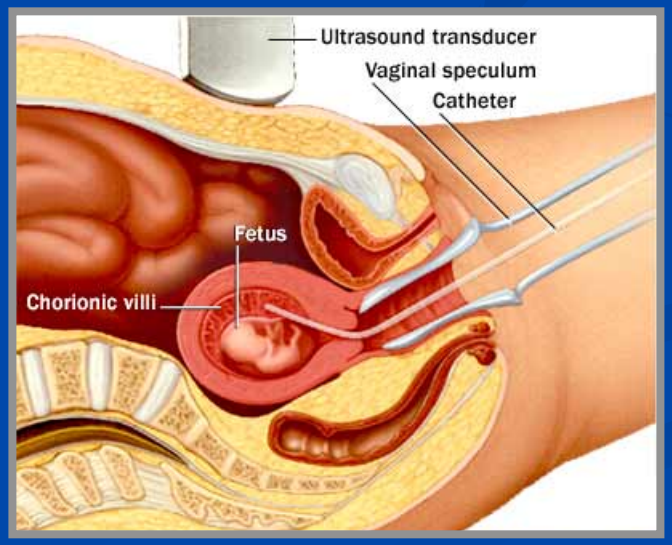
- 15-20 weeks gestation
- Quad Screen
  - Tests for AFP, hCG, uE3 and inhibin A
  - Neural tube defects, Down syndrome, Trisomy 18, Abdominal wall defects
  - Readjusts age-related risks

Prenatal Tests

- **Who is offered further testing?**
  - Advanced maternal age
  - Previous child or pregnancy with birth defect
  - Suggestive screening test results
  - Family history

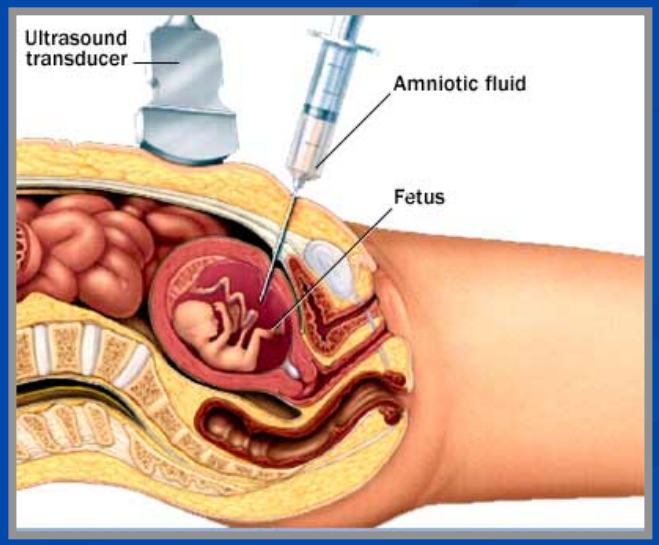
Prenatal Tests – CVS

- **Chorionic Villus Sampling**
  - 11-13 weeks gestation
  - Catheter/needle biopsy of placental cells
  - Performed through cervix or abdomen
  - Can test for chromosome and gene defects
  - 1-2% miscarriage rate
  - Digit/limb deficiencies (10 weeks)



Prenatal Tests - Amniocentesis

- Performed at 15-18 weeks gestation
- 10 cc amniotic fluid
- Living cells from fetus in amniotic fluid
- Cells grown in lab for 1-2 weeks
- Results in 3 weeks
- Chromosome and gene defects



Postnatal Testing

- Most done during first day of life
- Heel stick
- California (mandatory)
  - Galactosemia
  - Hypothyroidism (congenital)
  - Phenylketonuria (PKU)
  - Sickle Cell Disease (SCD) and Hemoglobinopathies
  - + 35 Others as of July, 2005

Postnatal Screening – Tandem Mass Spectrometry Screening Program

Fatty Acid Oxidation Disorders

- Carnitine/Acylcarnitine Translocase Deficiency (Translocase)
- Carnitine Palmitoyl Transferase Deficiency Type I (CPT-I)[2]
- 3-Hydroxy Long Chain Acyl-CoA Dehydrogenase Deficiency (LCHAD)
- 2,4-Dienoyl-CoA Reductase Deficiency[2]
- Medium Chain Acyl-CoA Dehydrogenase Deficiency (MCAD)
- Multiple Acyl-CoA Dehydrogenase Deficiency (MADD or Glutaric Acidemia-Type II)
- Neonatal Carnitine Palmitoyl Transferase Deficiency-Type II(CPT-II)
- Short Chain Acyl-CoA Dehydrogenase Deficiency (SCAD)
- Short Chain Hydroxy Acyl-CoA Dehydrogenase Deficiency (SCHAD)
- Trifunctional Protein Deficiency (TFP Deficiency)
- Very Long Chain Acyl-CoA Dehydrogenase Deficiency (VLCAD)

Organic Acid Disorders

- 3-Hydroxy-3-Methylglutaryl-CoA Lyase Deficiency (HMG)
- Glutaric Acidemia-Type I (GA I)
- Isobutyryl-CoA Dehydrogenase Deficiency
- Isovaleric Acidemia (IVA)
  - Acute onset
  - Chronic
- 2-Methylbutryl-CoA Dehydrogenase Deficiency
- 3-Methylcrotonyl-CoA Carboxylase Deficiency (3MCC Deficiency)
- 3-Methylglutaconyl-CoA Hydratase Deficiency
- Methylmalonic Acidemias
  - Methylmalonyl-CoA Mutase Deficiency 0
  - Methylmalonyl-CoA Mutase Deficiency +
  - Some Adenosylcobalamin Synthesis Defects
  - Maternal Vitamin B12 Deficiency
- Mitochondrial Acetoacetyl-CoA Thiolase Deficiency
  - (3-Ketothiolase Def.)
- Propionic Acidemia (PA)
  - Acute onset
  - Late onset
- Multiple-CoA Carboxylase Deficiency
- Malonic Aciduria

Amino Acid Disorders

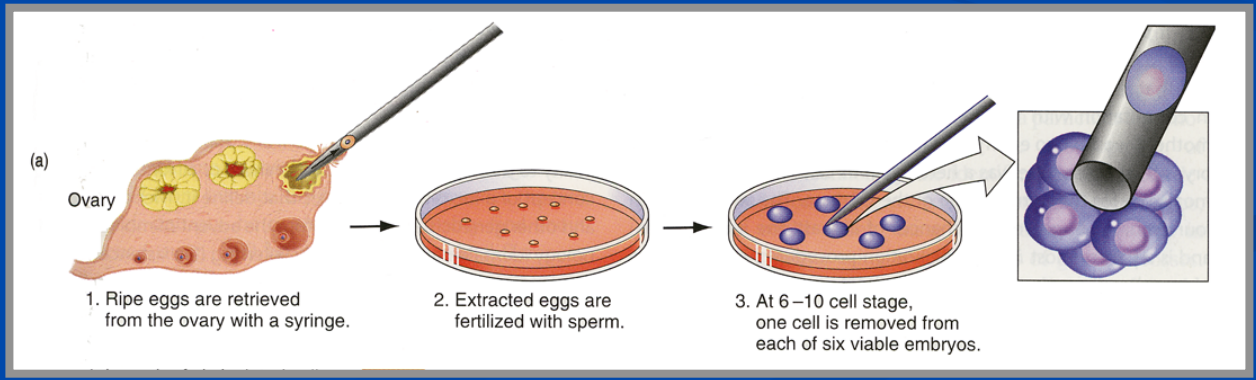
- Argininemia
- Argininosuccinic Aciduria (ASA Lyase Deficiency)
  - Acute onset
  - Late onset
- Carbamoylphosphate Synthetase Deficiency (CPS Def.)[2]
- Citrullinemia (ASA Synthetase Deficiency)
  - Acute onset
  - Late onset
- Homocystinuria
- Hypermethioninemia
- Hyperammonemia, Hyperornithinemia, Homocitrullinemia Syndrome (HHH)[2]
- Hyperornithinemia with Gyral Atrophy[2]
- Maple Syrup Urine Disease (MSUD)
  - Classical MSUD
  - Intermediate MSUD
- 5-Oxoprolinuria (pyroglutamic Aciduria)[2]
- Phenylketonuria (PKU)
  - Classical PKU
  - Hyperphenylalaninemia
  - Biopterin Cofactor Deficiencies (4)
- Tyrosinemia
- Transient Neonatal Tyrosinemia
  - Tyrosinemia Type I (Tyr I)[2]
  - Tyrosinemia Type II (Tyr II)
  - Tyrosimenia Type III (Tyr III)

Other Abnormal Profiles

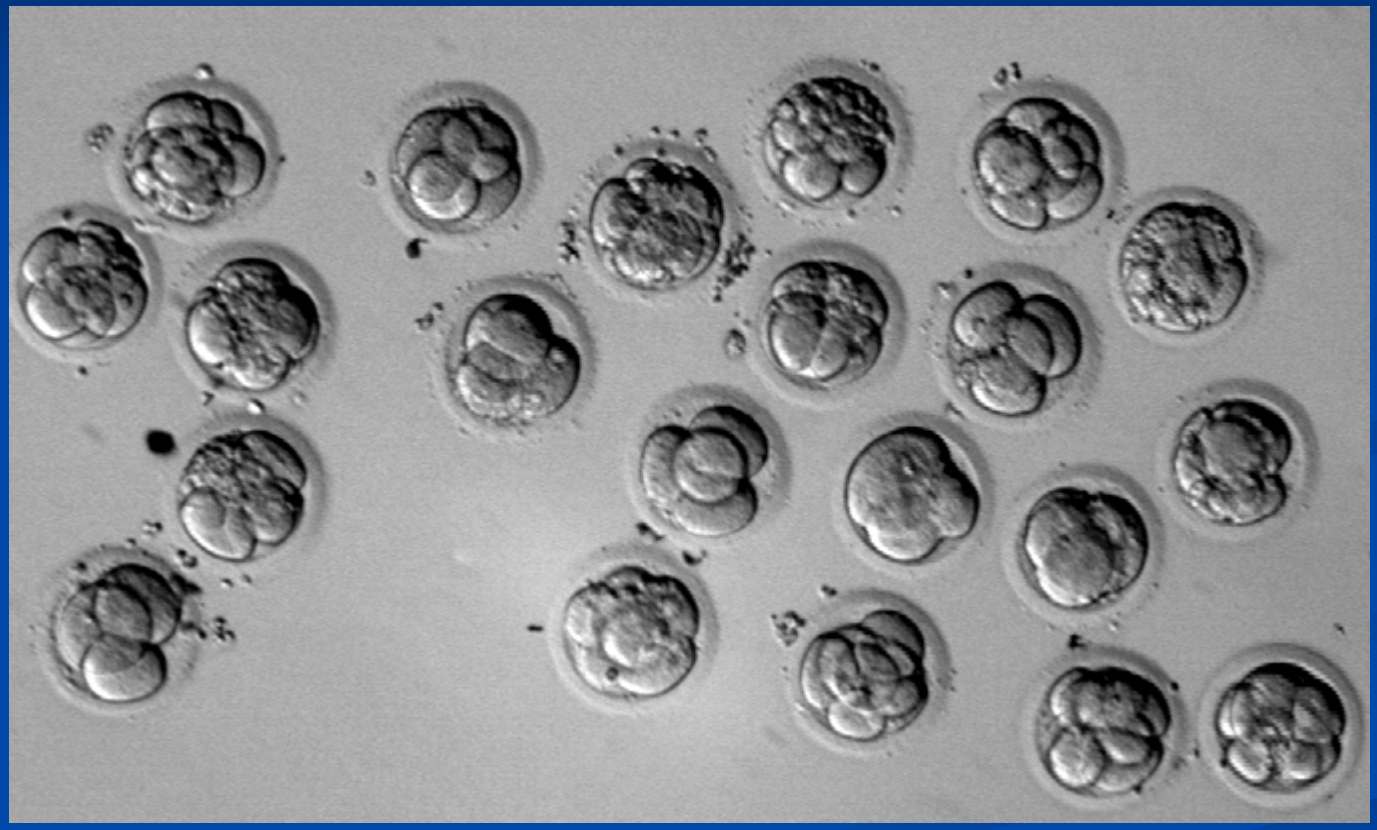
- Hyperalimentation
- Liver Disease
- Medium Chain Triglyceride (MCT) Oil Administration
- Presence of EDTA Antigoagulants in blood specimen
- Treatment with Benzoate, Pyvalic Acid, or Valproic Acid
- Carnitine Uptake Deficiency[2]

Preimplantation Genetic Screening (PGS)

- Can test embryos for genetic abnormalities prior to implantation
- Uses single cell (blastomere) at 8-cell stage



Which Embryo is Disease-Free?



PGS – Clinical Indications

- Single gene defects
- Balanced translocations
- Advanced maternal age (aneuploidy)
- Repetitive IVF failure
- Recurrent pregnancy loss
- Embryo selection

PGS

- Fluorescence in situ hybridization (FISH)
  - Aneuploidy/translocations and sexing (5-9 chromosomes)
- PCR
  - specific single gene disorders
- Gene Chips
  - many gene disorders & chromosomal abnormalities at one time

- Achondroplasia
- ADPKD1
- ADPKD2
- Adrenoleukodystroph
- Age-related aneuploidies
- Alpha-thalassemia
- Alpha-1-antitrypsin
- Alport disease
- Amyloid precursor protein (APP) mutation
- ARPKD
- Becker muscular dystrophy
- Beta-thalassemia
- Charcot Marie Tooth disease
- Chromosomal translocations
- Congenital adrenal hyperplasia
- Cystic fibrosis
- Down syndrome
- Duchenne muscular dystophy
- Dystonia
- Epidermolysis bullosa
- Familial dysautonomia
- Fanconi anemia
- FAP
- Fragile X syndrome
- Gaucher disease
- Hemophilia A and B
- HLA genotyping
- HSNF5 mutation
- Huntington disease
- Hypophosphatasia
- Incontinentia pigmenti
- Kell disease
- Klinefelter syndrome
- LCHAD
- Lesch Nyhan syndrome
- Marfan syndrome
- Multiple epiphysial dysplasia
- Myotonic dystophy
- Myotubular myopathy
- NF1 and NF2
- Norrie disease
- Osteogenesis imperfecta
- OTC deficiency
- P53 mutations
- PKU
- Retinitis pigmentosa
- SCA6
- Sickle cell anemia
- Sonic hedgehog mutations
- Spinal muscular atrophy (SMA)
- Tay-Sachs disease
- Tuberous sclerosis
- Turner syndrome
- Von Hippel Lindau
- X-linked hydrocephaly
- X-linked hyper IgM syndrome

PGS for Single Gene Disorders - Advantages

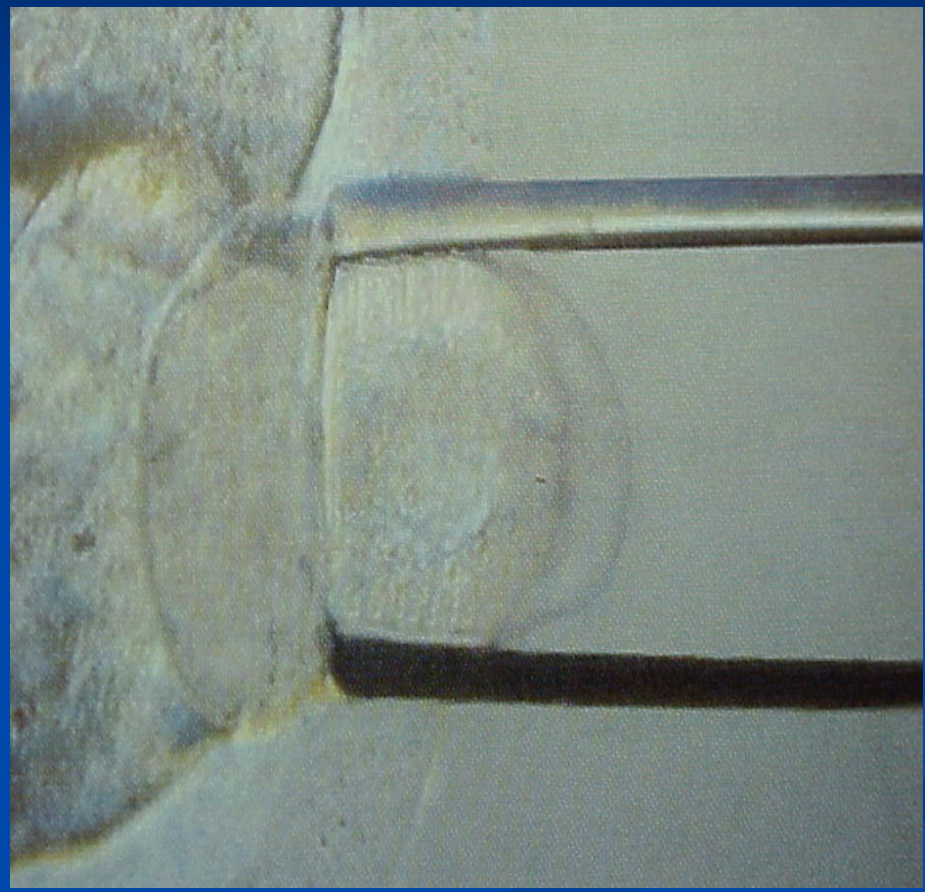
- Safer than elective termination
- More psychologically acceptable for couples
- Provides couples with another option
  - Adoption
  - Sterilization
  - Donor gametes

PGS

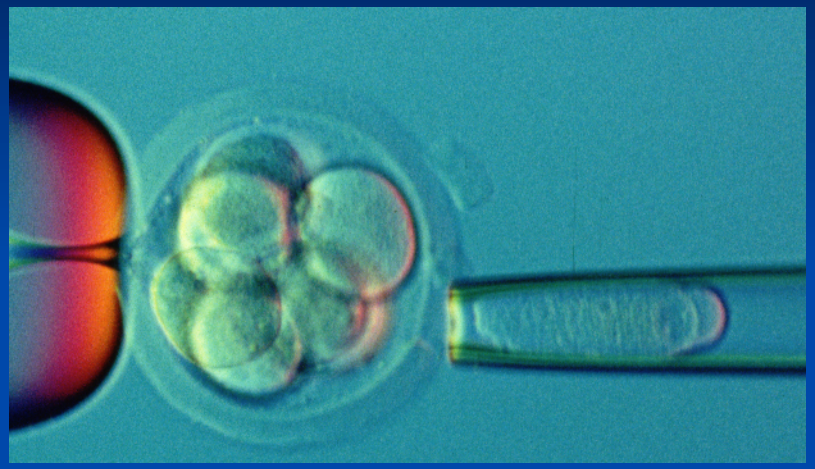
- *Pre-implantation genetic screening (PGS)* has been successfully used in diagnosing and preventing inherited genetic diseases like Cystic Fibrosis, Tay Sach's, Thalassemia, Sickle Cell Anemia and may be potentially used to screen for cancer mutations.

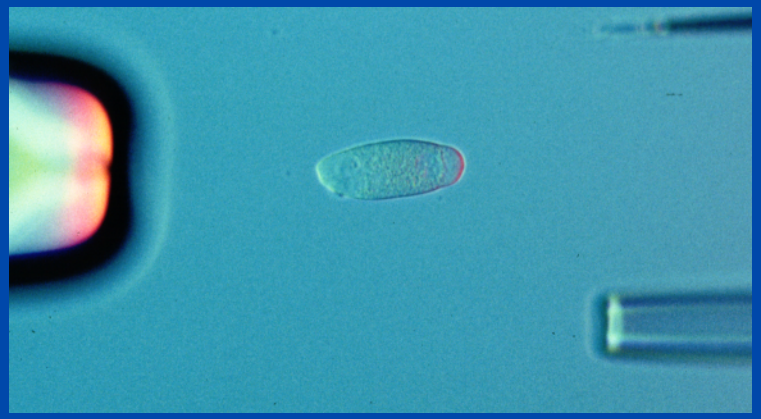
PGS

- After a cycle of in-vitro fertilization, biopsy of a single cell can be performed from an 8 cell embryo obtained after 3 days of culture in the laboratory.



PGS – Timing of Biopsy





- <67 hours post-retrieval
- Implantation rates significantly lower if >70 hours
- Probably represents technical issues with compacting embryo

PGS

- The genetic material of this single cell can be amplified by PCR and the chromosomal mutation or an aneuploidy can be identified in the embryo that underwent a biopsy.

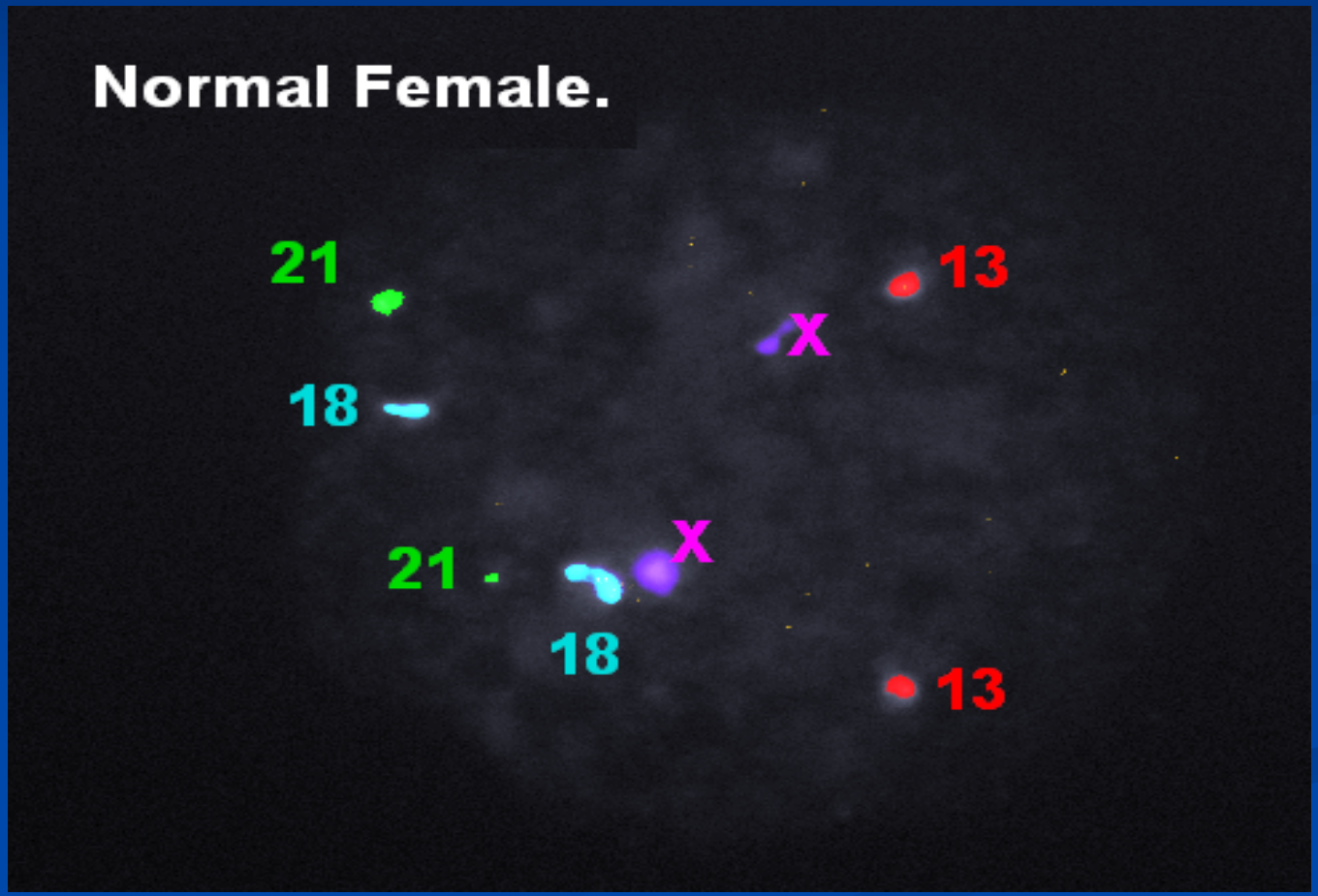
PGS

- The embryos would continue to grow for 2 more days in the laboratory, awaiting genetic analysis, and confirmation of which embryos were unaffected with the mutation or aneuploidy.

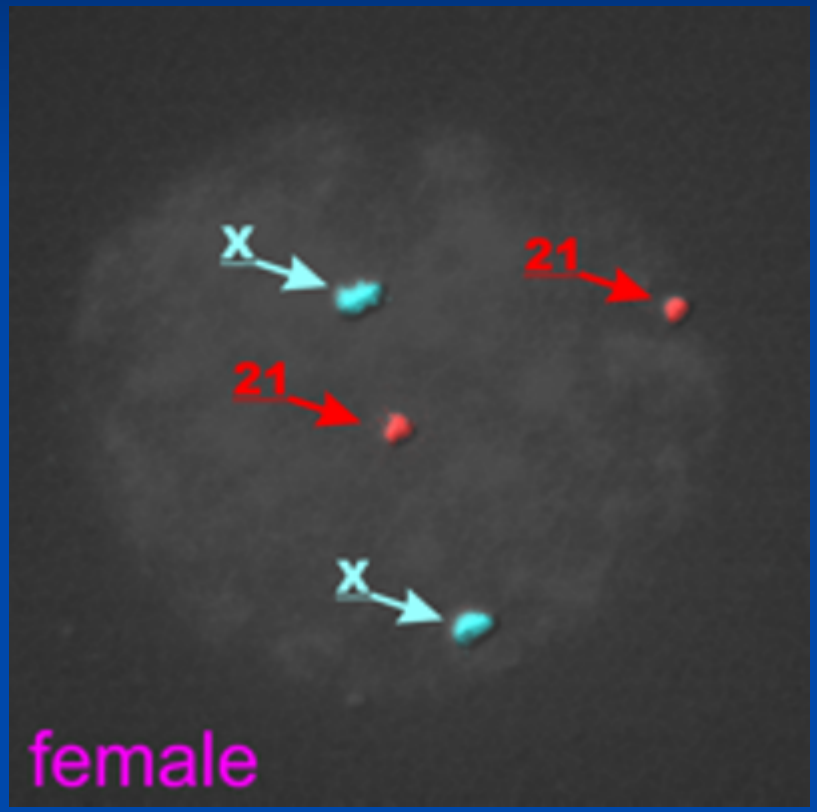
PGS

- The unaffected embryos are then transferred to the uterus at the blastocyst stage on day 5 of embryo culture and subsequently a child would be born unaffected from the screened genetic disease.

Five Chromosome PGD

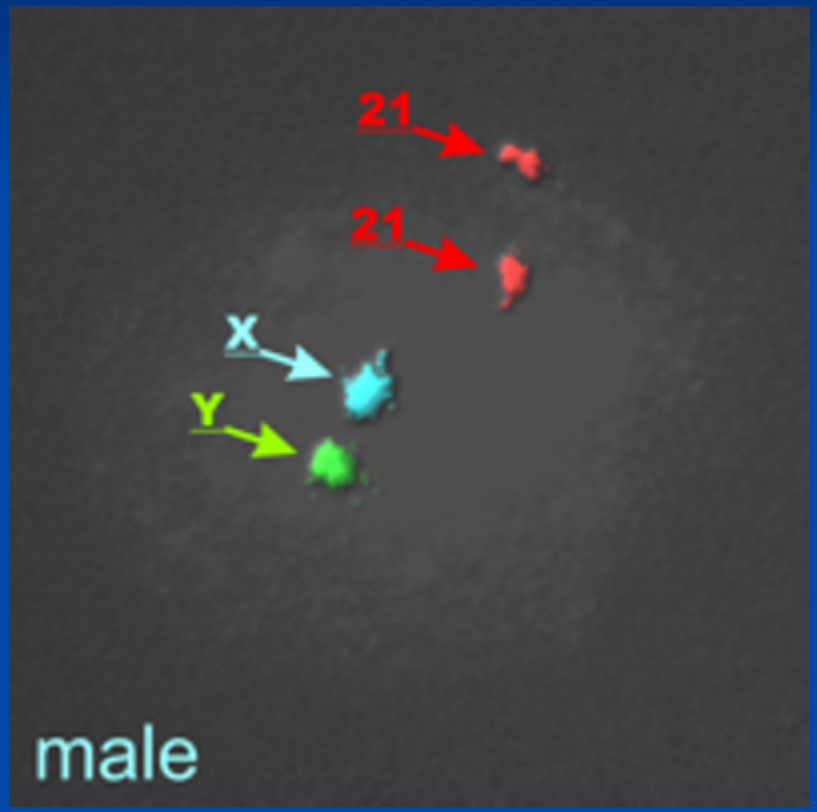


PGS – Female Embryo



- Uses fluorescence in-situ hybridization (FISH) technique to identify XX
- Sex-linked diseases
- "Family balancing"

PGS – Male Embryo



- Uses FISH to identify XY embryo

If you had one or more children of the same sex, would you like to be able to choose the gender of your next child?

a. Yes

b. No

Prenatal vs. Preimplantation Diagnosis

	PND	PGS
Cells	>100,000	1
Time	2 weeks	6-10 hrs
Accuracy	99%	99%
Cost	Covered	~$5,000

Who Would Benefit From PGS?

Couples with a history of --

- Abnormal numbers of chromosomes
- Single gene disorders
- Balanced translocations

Couples who --

- Desire an offspring of a certain sex

Future considerations

- Oocyte cryopreservation
  - "Pausing the biological clock"
- Cytoplasmic transfer
  - Donation of enucleated oocytes
- Reproduction without gametes
  - Use of nuclear material from somatic cells
  - Donated or synthetic cytoplasm
  - Reconstituted oocytes

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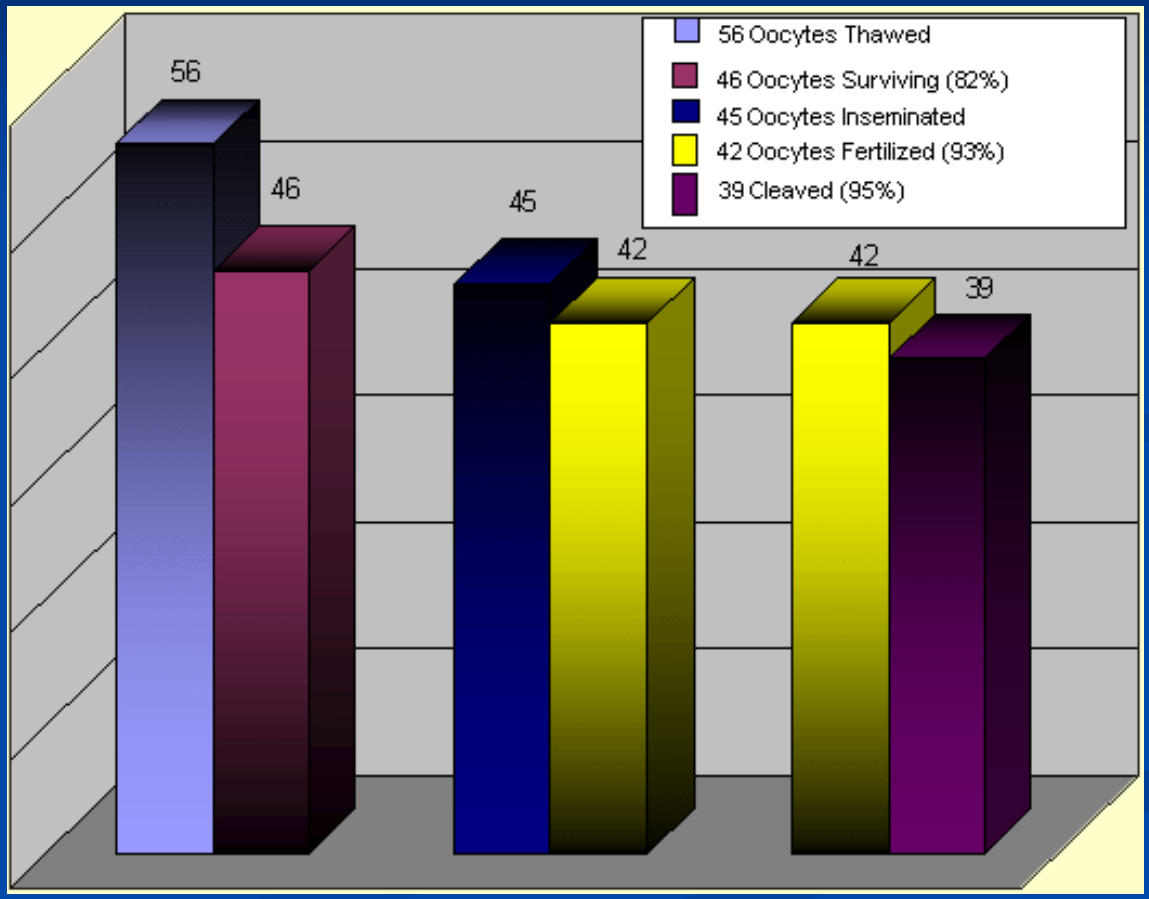

Questions??

- Sperm donor
- Female couple
- Huntington's disease
- Single woman
- Sex-linked disease
- Family balancing
- "Wrongful death" of discarded embryo
- Implantation of the wrong embryo

Thank you