

Medical Ethics & Professionalism II

Syllabus AY 2012-13 M'15

This course constitutes the second of your pre-clinical Ethics and Professionalism curriculum. The goals are the same as the first part:

- Engage in a self-reflective process of identifying personal moral values and their relevance to the medical profession
- Demonstrate how ethical considerations influence the practice of medicine and their far reaching implications for society, the profession, and lives of individual patients
- Encourage the open, free and respectful exchange of views by challenging simple moralistic dichotomies and emphasizing the pluralism and ambiguities inherent in the ethical practice of medicine
- Foster the development of ethically competent physicians capable of, and committed to, resolving day-to-day ethical conflicts through the reasoned and balanced application of ethical principles

Given the comparative brevity of the course, the overall competencies are more focused:

- Identify the unambiguous line separating professional from unprofessional attitudes and behaviors, while recognizing the ethically pluralistic nature of professional conduct
- Argue a given ethical position by identifying the relevant facts, weighing the ethical principles involved, and arriving at a defensible conclusion that justly balances all competing interests at stake
- Explain key events in the history of human experimentation, ethical principles governing human subjects research, and the roles of IRBs in overseeing research protocols
- Describe and apply the major legal and ethical principles governing the patient-physician relationship
- Identify common ethical conflicts experienced by medical students during their training, and explain how best to manage these conflicts when they inevitably arise

Student Responsibilities

Attendance

The course consists of three sessions, two of which are divided into a large group lecture immediately followed by a small group discussion. Attendance at all large and both small group sessions is required. To receive credit for attendance, you must click or sign in within the first 5 minutes of the session. If you need to miss

any session, be sure to you must contact the **Office of Student Affairs** before the session begins to receive an excused absence.

Reading Assignments

Reading assignments appear on TUSK under the relevant session. To insure a worthwhile discussion, please be sure to do the assigned readings in advance of the small group sessions.

Small Group Discussion Sessions

The class will be divided into approximately 17 small groups consisting of 12 students and 1 or 2 facilitators. You and your group will meet to discuss two different ethical topics. To prepare for these sessions, you will be provided with four cases to read and think about in advance. At the start of each session, your facilitator(s) will randomly select different students to present the relevant facts of each case and identify the applicable ethical principles. You are not required to submit anything in writing at the time of the small group sessions.

Student Evaluation

Your grade for the course will be solely based on your attendance and participation in the small group sessions. A single unexcused absence from either of these sessions will result in a failing grade for the course.

Faculty

Course Director

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Associated Course Director

Frank Chessa, PhD
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Lecturers

Andreas Klein, MD
Clinical Director, Lymphoma and Myeloma Service, Tufts Medical Center
Chair, Tufts Health Sciences Campus Institutional Review Boards

Marcia Boumil, MA MS JD LLM
Department of Public Health & Community Medicine
Tufts University School of Medicine

Course Schedule

Session	Format	Date / Time	Topic	Faculty
1	Large group lecture	October 20 1:00–2:30 pm	Research	Klein
2	Large group lecture	Dec 3/4* 9:10-10:20 am	Law & Medicine	Boumil
	Small group discussion	Dec 3/4 10:30-12:00 pm	Law & Medicine	Facilitators
3	Large group lecture	Feb 14 9:10-10:20 am	Assisted Reproductive Technology	Castellot
	Small group discussion	Feb 14 10:30-12:10 pm	Assisted Reproductive Technology	Facilitators

*The class is divided in half for these Monday and Tuesday morning blocks.

Session Information

Session 1

Research Ethics

Learning Objectives

- Identify key events in the history of human experimentation and major steps taken to protect the rights of human subjects
- Explain the ethical implications of obtaining informed consent for research subjects
- Describe the conflicts inherent in the role of physician as researcher
- Describe the roles of institutional review boards in overseeing research protocols and their execution

Reading Assignment

- The Nuremberg Code and Declaration of Helsinki
- Grady C. "Clinical Trials" in The Hastings Center Bioethics Briefing Book. 2008:21-24.

Session 2

Law & Medicine

Learning Objectives

By the end of this lecture, students will be able to:

- Identify and describe selected legal issues pertaining to the patient-physician relationship including bystander assistance, emergency services and termination of care
- Explain the elements of informed consent and legal obligations of physicians to preserve patient confidentiality
- Define defensive medicine and describe the motivating factors that encourage physicians to practice defensively
- Identify the relevant facts and use the appropriate ethical principles to argue a position in cases pertaining to conflicts in patient-physicians relationships

Reading Assignment

Discussion Cases

Cardiac Catheterization and Defensive Medicine
 HMO-Dictated Patient Discharge
 How Much Information Is Enough?
 When a Nonadherent Patient Needs Your Care

Learning Objectives

By the end of this lecture, students will be able to:

- Review the major technological innovations introduced to assist with reproduction since Louise Brown was conceived in vitro in 1977
- Identify the real and theoretical risks (physical and psychologic) to children born via assisted reproductive technology
- Explain the “paradox of harm”, and grapple with the argument that never to exist is sometimes preferable to its alternative
- Describe the ethical implications of pre-implantation genetic screening, including its potential to create “designer babies”
- Describe the practical and ethical implications of mature oocyte and embryo cryopreservation

Reading Assignment

Practice Committees of the American Society for Reproductive Medicine and the Society for Assisted Reproductive Technology. Mature oocyte cryopreservation: a guideline. *Ferti Steri* 2013 Vol 99(1):37-43

Discussion Cases

Sex Selection

Assisted Reproduction and *Primum Non Nocere*

Procrastinating Parents

Medical Research Ethics

Then and Now

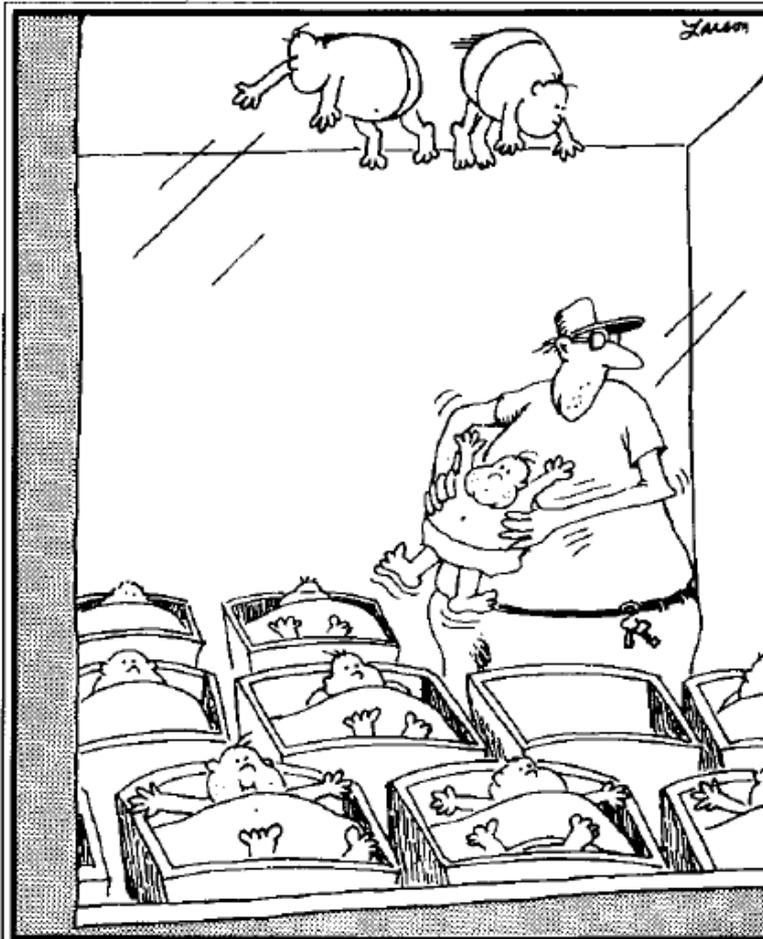
Andreas Klein, MD
Clinical Director, Lymphoma and Myeloma Services
Chair, Institutional Review Board
Tufts Medical Center
Tufts University Health Sciences

October 25, 2012

Objectives

- Review (brief) history of research ethics before and after WWII
- Understand basic tenets of human subjects research
- Discuss application of these principals to recent controversial research activities

Human Subjects Research



Late at night, and without permission, Reuben would often enter the nursery and conduct experiments in static electricity.

Medical Research Ethics

- Limited concern in society for welfare of research subjects prior to second world war
- “a *Cult of Medical Research*” in 1930’s celebrated researchers who experimented ... on others
- Opposition came from animal anti-vivisectionist equating animals and humans

Annals Int Med 1995; 123(2)

Nuremberg Trials: Nuremberg Code (1947)



The defendants at Nuremberg. Front row, from left to right: Hermann Göring, Rudolf Hess, Joachim von Ribbentrop, Wilhelm Keitel, Ernst Kaltenbrunner, Alfred Rosenberg, Hans Frank, Wilhelm Frick, Julius Streicher, Walther Funk, Hjalmar Schacht. Back row from left to right: Karl Dönitz, Erich Raeder, Baldur von Schirach, Fritz Sauckel, Alfred Jodl, Franz von Papen, Arthur Seyss-Inquart, Albert Speer, Konstantin van Neurath, Hans Fritzsche.

Courtesy of the National Archives.

Nuremberg Code (1947) - Condensed

1. voluntary consent of the human subject is absolutely essential
 - subject must be adequately informed and free to give consent
 - the duty to ascertain the quality of consent rests upon each individual who is involved in the experiment

Nuremberg Code (1947) - Condensed

2. Should be to the benefit of society and not obtainable by other means.
3. Should be designed and based on results of animal experiments and knowledge of the disease or problem that anticipated results will justify the experiment

Nuremberg Code (1947) - Condensed

4. Experiment should avoid all unnecessary physical and mental suffering and injury
5. No experiment should have a prior expectation of death or disabling injury*
6. Degree of risk should never exceed the humanitarian importance of the problem

Nuremberg Code (1947) - Condensed

7. Proper planning and facilities should protect against even remote possibility of injury, disability or death.
8. Experiment should be conducted only by qualified persons.
9. During experiment, subject may withdraw at any time
10. Scientist must be prepared to stop research if continuation of the experiment is likely to result in injury, disability or death.

United States of America v. Karl Brandt, et al.

- First of 12 trials for war crimes after WWII
- 20 of 23 were medical doctors, 3 others were Nazi officials
- All accused of involvement in Nazi human experimentation
- Trial held October 1946 – December 1947
- 7 received death sentence, 9 sentenced to prison 10 – life, 7 acquitted.

Unit 731 (1932-1945)

- Network of facilities established by Japanese in occupied China
- Run by academics, including pathologists
- Used political and other prisoners to test biological and chemical weapons
- 3000+ perished, no survivors



Unit 731

- At conclusion of war, Japan under exclusive US control; McArthur offered amnesty in exchange for data

Evidence gathered in this investigation has greatly supplemented and amplified previous aspects of this field. ... Such information could not be obtained in our own laboratories because of scruples attached to human experimentation. Hill, 1947

- Personnel captured by Russians prosecuted, sentenced to 2-25 years; remainder repatriated in 1950's
- Many Japanese returned to medical and research practice, some continuing experimentation



Henrietta Lacks

- b Aug. 1, 1920
- Dx'd with cervical cancer in 1951
- Samples taken by George Gey without consent
- Source of HeLa cell line

Ohio State Prison (1950s-1960s)



- Inmates at the Ohio State Prison, terminally ill patients, and 300 healthy women were injected with live HeLa cancer cells without being told

- Injections were given to 22 chronically ill, debilitated non-cancer patients to learn if foreign cancer cells would live longer in debilitated non-cancer patients than in patients debilitated by cancer.
- Research was funded by US Public Health Service Corps and the American Cancer Society

- Eventually, 3 young doctors refused to give the injections without telling patients in a nursing home they contained cancer cells. They reported their superiors and there was a trial.
- Mandel and Southam had their licenses suspended for a year
- The NIH required ethical review and informed consent agreements from human subjects going forward as condition of funding, but often ignored

Public Announcement

WE WILL PAY YOU \$4.00 FOR ONE HOUR OF YOUR TIME

Persons Needed for a Study of Memory

*We will pay five hundred New Haven men to help us complete a scientific study of memory and learning. The study is being done at Yale University.

*Each person who participates will be paid \$4.00 (plus 50c carfare) for approximately 1 hour's time. We need you for only one hour: there are no further obligations. You may choose the time you would like to come (evenings, weekdays, or weekends).

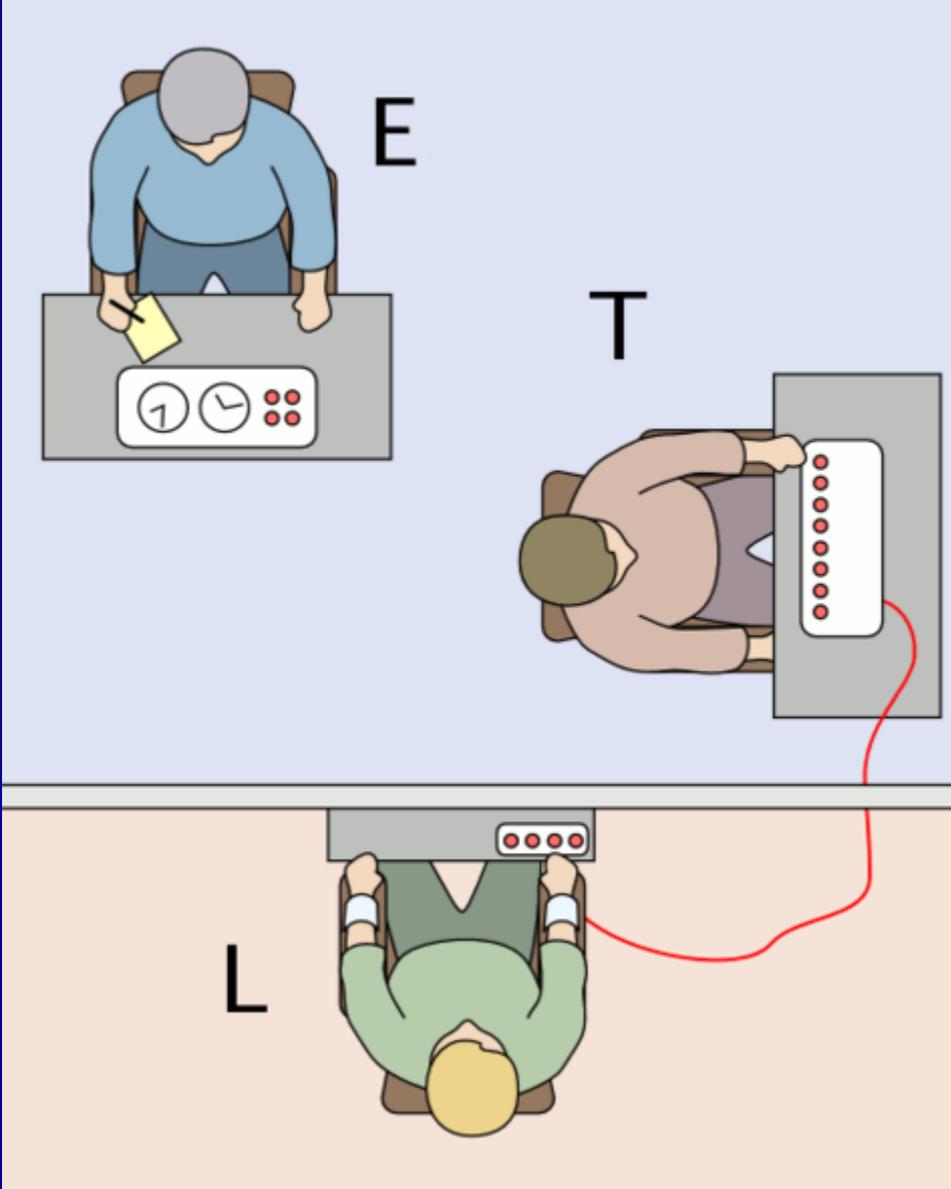
*No special training, education, or experience is needed. We want:

Factory workers	Businessmen	Construction workers
City employees	Clerks	Salespeople
Laborers	Professional people	White-collar workers
Barbers	Telephone workers	Others

All persons must be between the ages of 20 and 50. High school and college students cannot be used.

*If you meet these qualifications, fill out the coupon below and mail it now to Professor Stanley Milgram, Department of Psychology, Yale University, New Haven. You will be notified later of the specific time and place of the study. We reserve the right to decline any application.

*You will be paid \$4.00 (plus 50c carfare) as soon as you arrive at the laboratory.



Milgram research (1961)



Stanley Milgram, PhD Obedience Shock Generator

Research laboratory at Yale University

Before...



...and after.



The New England Journal of Medicine

Copyright, 1966 by the Massachusetts Medical Society

Volume 274

JUNE 16, 1966

Number 24

Reprinted from pages 1354-1360.

SPECIAL ARTICLE

ETHICS AND CLINICAL RESEARCH*

HENRY K. BEECHER, M.D.†

BOSTON

- Pointed out significant ethical lapses in 22 studies published in major journals in 1964
 - Inadequate consent
 - Inappropriate procedure risks
 - withholding treatment

Declaration of Helsinki

- Created in 1964; revised 1975, 1983, 1989, 1996, 2000



“A view of the Market Square, the white Supreme Court of Finland, the brown Swedish Embassy, the blue Helsinki City Hall and Helsinki Cathedral in the background. The Kallio church tower is also visible in the background on the far right.” *Courtesy of Wikipedia*

Declaration of Helsinki

- Ratified by World Medical Association
- Affirms primacy of physician's role in protecting patients
- Affirms ongoing need for research to improve knowledge of disease
- Guide for the proper conduct of research for physicians and sponsors

Macon County Health Department

ALABAMA STATE BOARD OF HEALTH AND U. S. PUBLIC HEALTH
SERVICE COOPERATING WITH TUSKEGEE INSTITUTE

Dear Sir:

Some time ago you were given a thorough examination and since that time we hope you have gotten a great deal of treatment for bad blood. You will now be given your last chance to get a second examination. This examination is a very special one and after it is finished you will be given a special treatment if it is believed you are in a condition to stand it.

If you want this special examination and treatment you must meet the nurse at _____ on _____ at _____ M. She will bring you to the Tuskegee Institute Hospital for this free treatment. We will be very busy when these examinations and treatments are being given, and will have lots of people to wait on. You will remember that you had to wait for some time when you had your last good examination, and we wish to let you know that because we expect to be so busy it may be necessary for you to remain in the hospital over one night. If this is necessary you will be furnished your meals and a bed, as well as the examination and treatment without cost.

REMEMBER THIS IS YOUR LAST CHANCE FOR SPECIAL FREE TREATMENT. BE SURE TO MEET THE NURSE.

Macon County Health Department

Letter from
Marion County
Health Dept.
inviting men
with “bad
blood” to attend
a visit for
“special free
treatment”
which was
actually a
diagnostic
spinal tap.

Tuskegee Syphilis research (1932-1972)



**Members from the CDC perform
“back shots” (spinal taps), 1933**



**A procedure among the
“treatments” received**

- Funded by US Public Health Service to study natural history of syphilis
- Started in 1932 when no effective treatment available
- Enrolled 399 indigent and uneducated AA sharecroppers in Macon County, Alabama

Tuskegee Syphilis research (1932-1972)

- By mid-1940's, penicillin known effective, but actively withheld from participants who believed they were receiving treatments
- Only stopped after whistleblower brought to media attention in 1972
- *"The men's status did not warrant ethical debate. They were subjects, not patients; clinical material, not sick people."*
- \$10M payout followed

Tuskegee Syphilis research (1932-1972)

- By the end of the experiment
 - 28 men had died directly of syphilis
 - 100 men were dead of related complications
 - 40 of their wives had been infected
 - 19 of their children had been born with congenital syphilis

May 1997, President Clinton apologized to the surviving victims at a White House ceremony: Sam Doner, Ernest Hendon, Carter Howard, George Key, Frederick Moss, Charlie W. Pollard, Herman Shaw, and Fred Simmons.



Origins of the IRB

National Research Act (1974)

- Created IRB framework
 - DHHS promulgated 45 Code of Federal Regulations (CFR) 46 (1980s, revised 2001)
 - Adoption of 45 CFR 46 by 17 federal agencies: the Common Rule (1991)
- Created The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research
 - Belmont Report (1979)



Belmont: Applying Ethical Principles

Respect for Persons: Autonomy

- Informed consent
- Voluntary participation
- Freedom to withdraw without penalty
- Protect privacy and confidentiality

Belmont: Applying Ethical Principles

Beneficence: “*Do unto others...*”

- Risks are minimized; benefits are maximized
- Risks are justified by potential benefits
- Conflicts of interest are managed or eliminated

Belmont: Applying Ethical Principles

Justice: Distribute Risks and Benefits

- Protection of vulnerable populations
- Those who may benefit are not excluded

Regulations and Policies



- **OHRP: 45 CFR 46**
- **FDA: 21 CFR 50, 56, 312, 812**
- **State:**
 - **Vary state to state**
 - **MA Fetal Research Statute**
- **Be familiar with institutional policies**



Problem solved?

Belmont: Applying Ethical Principles

Respect for Persons: Autonomy

- Informed consent
- Voluntary participation
- Freedom to withdraw without penalty
- Protect privacy and confidentiality



EXPERIMENTS IN TORTURE:

Evidence of Human Subject
Research and Experimentation
in the "Enhanced" Interrogation Program

Physicians for Human Rights, June 2010

Terror Investigations

- Following attacks on Sept 11, 2011, US Gvt stepped up intelligence gathering
- Justice Dept Office of Legal Council redefined certain acts (waterboarding, extreme sleep deprivation, stress positioning) as “safe, legal and effective” under rules of “enhanced interrogation techniques”

Enhanced Interrogation

- Required medical personnel to monitor EIT, ostensibly to ensure did not cause “severe mental or physical pain”
- Accusation: CIA systematically used information obtained to enhance “safety” and effectiveness

Waterboarding

- Medical service instructed to record:
...how long each application (and the entire procedure) lasted, how much water was applied (realizing that much splashes off), how exactly the water was applied, if a seal was achieved, if the naso- or oropharynx was filled, what sort of volume was expelled, how long was the break between applications, and how the subject looked between each treatment.

Waterboarding

- CIA already knew using saline rather than water reduced hyponatremia from 1960's
- Improvements:
 - Liquid / soft diets to avoid aspiration
 - Tracheostomy kit on site

Susceptibility to Pain

- Interrogators applied various techniques simultaneously vs. sequentially to determine if pain threshold changed
- Developed procedures based on experience with at least 25 detainees

Susceptibility to Pain

- Conclusion

“OMS doctors and psychologists, moreover, confirm that they expect that the techniques, when combined as described in the *Background Paper* and in the *April 22 [redacted] Fax*, would not operate in a different manner from the way they do individually, so as to cause severe pain”

Memorandum from Steven G. Bradbury, Principal Deputy Assistant Attorney General, for John A. Rizzo, Senior Deputy General Counsel, Central Intelligence Agency (10 May 2005)

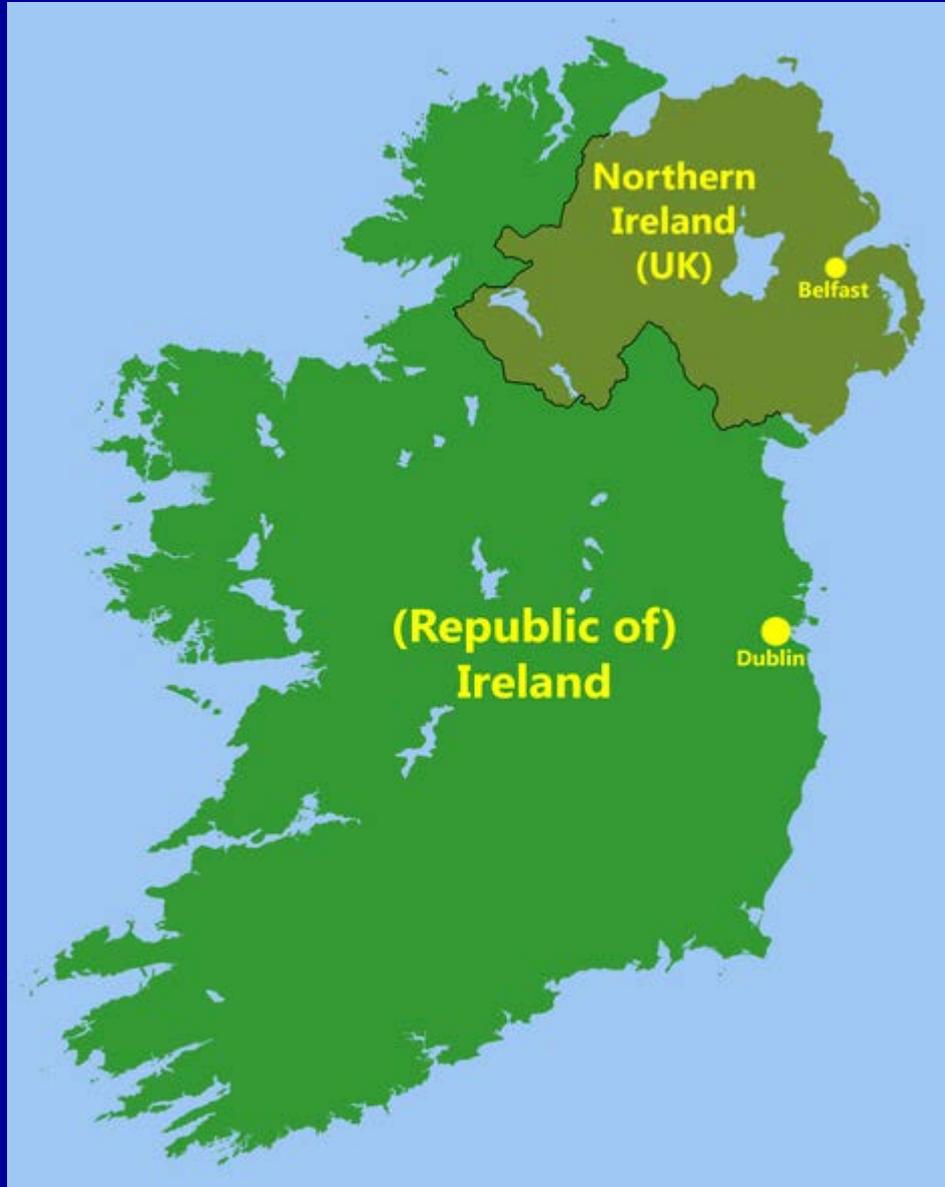
Questions

- Did CIA conduct a systematic investigation to develop generalizable knowledge to guide future “Enhanced Interrogations” on detainees?
- Could consent obtained in these circumstances ever be valid?
- What was role of medical personnel in the procedures – ensuring “safety” or engaged in research?

Belmont: Applying Ethical Principles

Beneficence: “*Do unto others...*”

- Risks are minimized; benefits are maximized
- Risks are justified by potential benefits
- Conflicts of interest are managed or eliminated



The Troubles

- Secessionist movement in Northern Ireland pitting predominantly Nationalist/Catholic groups favoring independence from England (IRA) versus predominantly Unionist/Protestant groups (Orange Order) favoring the UK.
- Violent protests, bombings, executions, reprisals & recriminations over 3 decades

Belfast “Good Friday” Agreement

- Negotiated by George Mitchell (D), ME
- Ratified by popular referendums in Northern Ireland and Republic of Ireland in 1998
- Negotiated halt to hostilities & disarming of militant groups
- Integration into political system

Belfast Project

- Oral history project at Boston College initiated by journalist Ed Moloney and former IRA member Anthony McIntyre begun in 2001
- Interviewed key players on both sides
- Interviews granted on condition that would not release interviews until participant had died
- [date] released first book based on testimony of .

Belfast Project

- Dolours Price, subject of interview, reportedly confessed involvement in murder of Jean McConville, accused informant for British Gov't in 1972
- Revealed involvement in *BP* in violation of confidentiality agreement with BC
- British Gov't re-opened case and subpoenaed interview transcripts & tapes under terms of mutual aid treaty with US

Feds subpoena interviews of IRA members from Boston College oral history project

Posted by Martin Finucane May 13, 2011 01:09 PM

Print | Comments (0)

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E-mail

By Tracy Jan, Globe Staff

Boston College officials say they're examining a subpoena from reportedly seeking confidential interviews of two members of the Republican Army collected in the 1990s as part of an oral history project in Northern Ireland.

"Boston College is reviewing the subpoena from the US Attorney for additional information in light of the ramifications it poses regarding the interviews and the impact on oral history projects as an academic spokesman Jack Dunn said today in an emailed statement.

The New York authorities are... Ireland believe... country

Court hears of possible threat to researchers in BC case

April 05, 2012 | By Martine Powers

THIS STORY APPEARED IN **The Boston Globe**

Twitter Tweet < 13

+1 < 0

Print

Researchers responsible for a high-profile oral history project will probably face violent retaliation if Boston College relinquishes confidential interviews with former members of the Provisional Irish Republican Army, a lawyer argued in federal appeals court Wednesday.

But lawyers for the US government contend that an international treaty on criminal



Ed Moloney and Carrie Twomey, wife of former IRA member Anthony McIntyre,.... (Jessica Rinaldi /Reuters)

Boston College can't keep IRA materials confidential

July 07, 2012 |

THIS STORY APPEARED IN **The Boston Globe**

Twitter Tweet < 0

Print

A federal appeals court has upheld a lower court's ruling ordering Boston College to turn over confidential materials from its Belfast Oral History Project on Northern Ireland, dealing a blow to researchers' efforts to honor their agreement of secrecy with former IRA members.

The decision by the US Court of Appeals for the First Circuit was released Friday and reinforces subpoenas from the British government that would force BC to release specific papers and interviews conducted by researchers. Two of the academic researchers in the appeal were project director Ed Moloney and former Irish Republican Army member Anthony McIntyre.

anded the records

'project, an effort to rn Ireland.

r subjects that the

Belfast Project

- BC lost initial attempt to block subpoena and did not file appeal
- Researchers resisting on basis of perceived danger to themselves and research subjects and First Amendment privilege
- Reopening of old wounds
- Receives temporary stay of court ruling from Supreme Court Justice Breyer to allow time to prepare arguments for appeal

Questions

- Were subjects adequately informed of risks?
- Were adequate measures taken to address safety of participants?
- Who can grant anonymity / guarantee confidentiality?
- What is the boundary between research and journalism?

Belmont: Applying Ethical Principles

Justice: Distribute Risks and Benefits

- Protection of vulnerable populations
- Those who may benefit are not excluded

Huntington's Disease

- Autosomal dominant genetic disorder of Huntingtin gene
- Results in progressive neurologic deterioration by age 30's in all affected
- No cure, treatment palliative, death inevitable
- Symptoms can appear after peak childbearing age -> to have children or not?

Search for Cause

- Genetic polymorphism association studies hit on the 12th try, localized to short arm Chr4 in 1983
- Gene identified and mutation defined in 1993
- Research continues to understand pathogenesis of disease and potential treatments

Huntington's Kindreds

- Success of genetic linkage analysis relies on size and quality of family information
- Limited kindreds identified in US
- Largest kindred in Lake Maracaibo, Venezuela with 3000 members since early 1800's traceable to single ancestor

Huntington's Progress

- Researchers spent months obtaining blood samples and pedigree information
- Identification of gene led to development of genetic test to predict HD
 - Available widely in US and Europe
 - Costs ~\$1000
- Potential treatments include siRNA and other \$\$\$ approaches

Questions

- Who has benefited from this research?
- Are Venezuelan families likely to benefit from future treatments?
- Nancy Wexler, MD has raised \$6M for care in Venezuela – is this enough?



M'15 Medical Ethics & Professionalism II
Small Group Discussion Cases – Student Version
Session 2: December 3 and 4, 2012

(1) Cardiac Catheterization and Defensive Medicine

Mr. Damon, a 62-year-old man with known coronary artery disease and a long history of angina, came to see his cardiologist, Dr. Ross, with chest pain—again. Such complaints had been typical during Mr. Damon's clinic visits over the last two years. Each episode was brought on by physical exertion and, just as predictably, was relieved with rest and a nitroglycerin tablet. Previous stress tests and cardiac catheterizations had shown the presence of stable angina without major blockages or areas of ischemia. Dr. Ross did his usual evaluation of Mr. Damon and concluded that Mr. Damon was having his typical angina, needed no changes to his medications, and did not need invasive cardiovascular testing.

As he was about to send Mr. Damon home, he remembered a fellow cardiologist who, in a similar clinical situation, sent a patient home without a cardiac catheterization. That patient died shortly thereafter of a heart attack, and the patient's family attempted to sue the physician for malpractice. Dr. Ross's clinical judgment told him that further testing was unnecessary, but he was concerned that such judgment alone might not hold up in court. While he knew that many of his colleagues would agree with his clinical assessment, he also knew that others would order a catheterization to protect themselves from potential litigation. Dr. Ross was worried about the complication risk of feeding a catheter up through the femoral artery into the heart and injecting dye into the coronary arteries, and he also wondered about the added strain on Mr. Damon's finances.

American Medical Association Journal of Ethics October 2010, Volume 12, Number 10.

(2) Medical Culture and Error Disclosure

Dr. Jackson and his resident, Kim, were performing surgery on Mr. Frank, a patient with recurrence of a metastatic germ cell tumor. The standard of care for this surgery includes retroperitoneal lymph node dissection. Before the surgery, Dr. Jackson told Mr. Frank about the procedure and its risks, benefits, and alternatives. Mr. Frank was made aware that the surgery carried significant risk of bleeding and the need for blood transfusions; his informed consent to the surgery was documented and placed in the medical record.

During the lymph node dissection, several small blood vessels were inadvertently severed, and Mr. Frank lost enough blood to require a transfusion of one unit of red blood cells. Although Mr. Frank's blood pressure was borderline low for several minutes during surgery, the procedure was completed without other complications, the remaining tumor and lymph nodes were removed, and Mr. Frank emerged from anesthesia in good condition.

Before Kim left the operating room, she told Dr. Jackson she would speak with the patient's family and let them know that the surgery went well and that Mr. Frank had received a blood transfusion because several vessels had been cut.

Dr. Jackson responded, "There's no need to inform them of the nicked vessels. Patients know that bleeding and blood transfusions are a risk of the surgery, and Mr. Frank was no exception. He signed the consent saying he was aware of these risks. If we told patients every time something unplanned happened in medicine, we would spend all our time defending lawsuits. Patients simply aren't capable of understanding the idiosyncrasies of medicine. I've talked to my malpractice insurance company and a malpractice attorney about these types of situations. They both advised me that when something happens like this that's not a black-and-white error there's no need to tell the whole story unless there's some lasting effect, or I think it's in the best interest of patient care. All that we need to do is tell Mr. Frank and his family that he lost a lot of blood and needed a transfusion."

Kim spoke with the family immediately after the procedure and informed them that the surgery went well, with only a minor complication that involved some blood loss and the need for a transfusion. Several hours later, Dr. Jackson gave Mr. Frank the same explanation.

Having recently attended a training session with the hospital risk management department, Kim knew that the hospital had a policy of full disclosure when there were clear medical errors. She had even heard that lawsuits might occur less frequently if physicians disclosed their errors and apologized. But she was not sure that this situation qualified as a clear error, whether she was obligated to contact risk management, what the consequences might be for her and Dr. Jackson if she didn't report this, or whether she might face a lawsuit if the patient found out about the nicked vessels.

When Kim saw Mr. Frank the next day, she reiterated what Dr. Jackson had said about the surgery. Mr. Frank asked her if he would recover from the blood loss okay, and Kim stated that he might feel a little more tired than usual for a few days and that the blood loss might delay his recovery by a day or two, but that the blood loss would not affect his ability to make a full recovery.

American Medical Association Journal of Ethics May 2008, Volume 10, Number 5: 282-287.

(3) When a Nonadherent Patient Needs Your Care

Dr. Jefferson, an OB/GYN in private practice, first took care of Ms. Carr when her mother brought the 15 year-old girl in for a pregnancy evaluation. The test was positive, and Ms. Carr's mother accompanied her daughter on every prenatal visit. After a successful delivery, Dr. Jefferson brought up the topic of birth control. Ms. Carr, partly on the insistence of her mother, wanted to take birth control pills because she had heard that they improved one's complexion and didn't cause much weight gain. Concerned about the 15-year-old's ability to stick with a contraceptive that required daily vigilance, Dr. Jefferson suggested taking a longer acting

contraceptive, but Ms. Carr insisted that birth control pills were the only kind of contraceptive she wanted.

Over the next 3 years, Dr. Jefferson saw Ms. Carr for routine care, including renewing her prescription for birth control pills, always accompanied by her mother. One day, she came in without her mother; and Dr. Jefferson learned that the 2 had had a falling out and Ms. Carr had moved in with her boyfriend.

Ms. Carr missed a scheduled appointment, and when Dr. Jefferson saw her again, she was several weeks pregnant. When asked why she had missed her appointments, Ms. Carr replied that she couldn't make it at the scheduled time and didn't think that missing an appointment was such a big deal—she wanted to get pregnant. During the visit, Dr. Jefferson stressed the importance of prenatal care for the health of both Ms. Carr and her baby and the need for Ms. Carr to come to all her scheduled appointments.

Ms. Carr made her next appointment before she left the office but she failed to keep it. She did not respond to several calls prompted by Dr. Jefferson's tickler file for women receiving prenatal care. Four months into her pregnancy, Ms. Carr appeared without an appointment. When asked about the missed appointment, Ms. Carr apologized. "I know I should have come, but I have a job and another child to take care of and now that I live with my boyfriend, your office is much farther away than when I lived with my mother. I can't take off work without being docked and I can't leave the 3-year-old after I get home. I knew you needed to see me." Dr. Jefferson was worried about how Ms. Carr looked; she had gained too much weight. Dr. Jefferson went ahead and saw her at the unscheduled time. She did an exam and got blood work. She sent Ms. Carr away with a printed diet that called for less salt, decreased carbohydrates, and fewer calories in general.

The lab work showed that Ms. Carr's blood sugar was elevated, so Dr. Jefferson had the office secretary call to schedule an urgent appointment because of concerns about gestational diabetes and its potential negative impact on the fetus. Despite repeated attempts to contact her, Ms. Carr didn't return to the doctor's office until 4 weeks later, now 5 months pregnant. She had gained more weight and had some swelling in her ankles. Dr. Jefferson informed her of the importance of closely monitoring and treating her diabetes, and that it might be better if Ms. Carr found a physician closer to home or work whom she could get to more regularly. Dr. Jefferson said that Ms. Carr's last trimester should be monitored carefully and that she, Dr. Jefferson, would help Ms. Carr find another physician. Two weeks later, Dr. Jefferson was happy to receive a request from a colleague for Ms. Carr's medical records.

One month later, Dr. Jefferson received a call from labor and delivery at a hospital where she attends. A nurse's aide said that Ms. Carr had showed up at the ER in premature labor and had been admitted. When asked who her doctor was, Ms. Carr promptly gave Dr. Jefferson's name.

(4) How Much Information Is Enough?

Dr. Anderson glanced at the clinic schedule and saw that Mr. Taylor, a new patient, was next on his schedule. Mr. Taylor was a man in his mid-20s who had come to the clinic for treatment of a nagging respiratory virus. After finding out that Mr. Taylor had no medical home and hadn't had a check-up in the last few years, Dr. Anderson took a detailed history, during which he learned that Mr. Taylor was gay, and, while he'd had other partners in the past, had recently settled down with a man whose companionship he valued and whom he considered to be his life partner. Dr. Anderson explained that since Mr. Taylor had not seen a doctor in a while and was not feeling well, he'd like to do a physical exam and order some blood work. When it came to ordering the blood work, Dr. Anderson asked Mr. Taylor, "When did you last have an HIV test?"

"I've never had one and neither has my partner, Dave. Both of us have always been careful in the past. Do you really think it's necessary?"

"Yes I do," Dr. Anderson replied. "Especially now that you and Dave want to make a life with each other. It will give you both the information you need. I can order the HIV test along with the other blood work we need to check out these symptoms."

"OK," Mr. Taylor agreed.

Dr. Anderson hesitated for a moment, debating his next step. How would Mr. Taylor react if he learned about the consequences of that test—specifically that Dr. Anderson would have to report an HIV-positive result to the public health department and insist that Mr. Taylor tell his partner (or risk Dave finding out from public health officials)?

Dr. Anderson worried that Mr. Taylor would not agree to the test if he had all of this information. He considered not telling Mr. Taylor, thinking he might justify this omission in the interest of safety for third parties—Dave and possibly others. Mr. Taylor might get up and leave the clinic if Dr. Anderson told him about the reporting duty, and he might not seek treatment elsewhere. If it came to that, Dr. Anderson thought, he could tell Mr. Taylor about the reporting requirement next time, when the results were in. There was, after all, a 50-50 chance he would have nothing to report.

Assisted Reproductive Technology

Milestones in ART and IVF

- 1978** Louise Brown born in U.K.
- 1981** Elizabeth Carr born in U.S.
- 1990** First births from frozen embryos
- 1997** Dolly is born
- 1998** Human embryonic stem cells produced
- 1999** Natalie Brown (Louise's sister) is first IVF baby to have a naturally conceived baby; Louise has also had a naturally conceived baby
- 2002** Adult stem cells are multipotent
- 2002** Two millionth ART baby born in U.S. (one million via IVF)
- 2004** Fetal cord blood stem cells are multipotent
- 2008** Roughly 2% of all U.S. births are via IVF
- 2012** Four millionth ART baby born, nearly three million in U.S.



How is Infertility Defined?

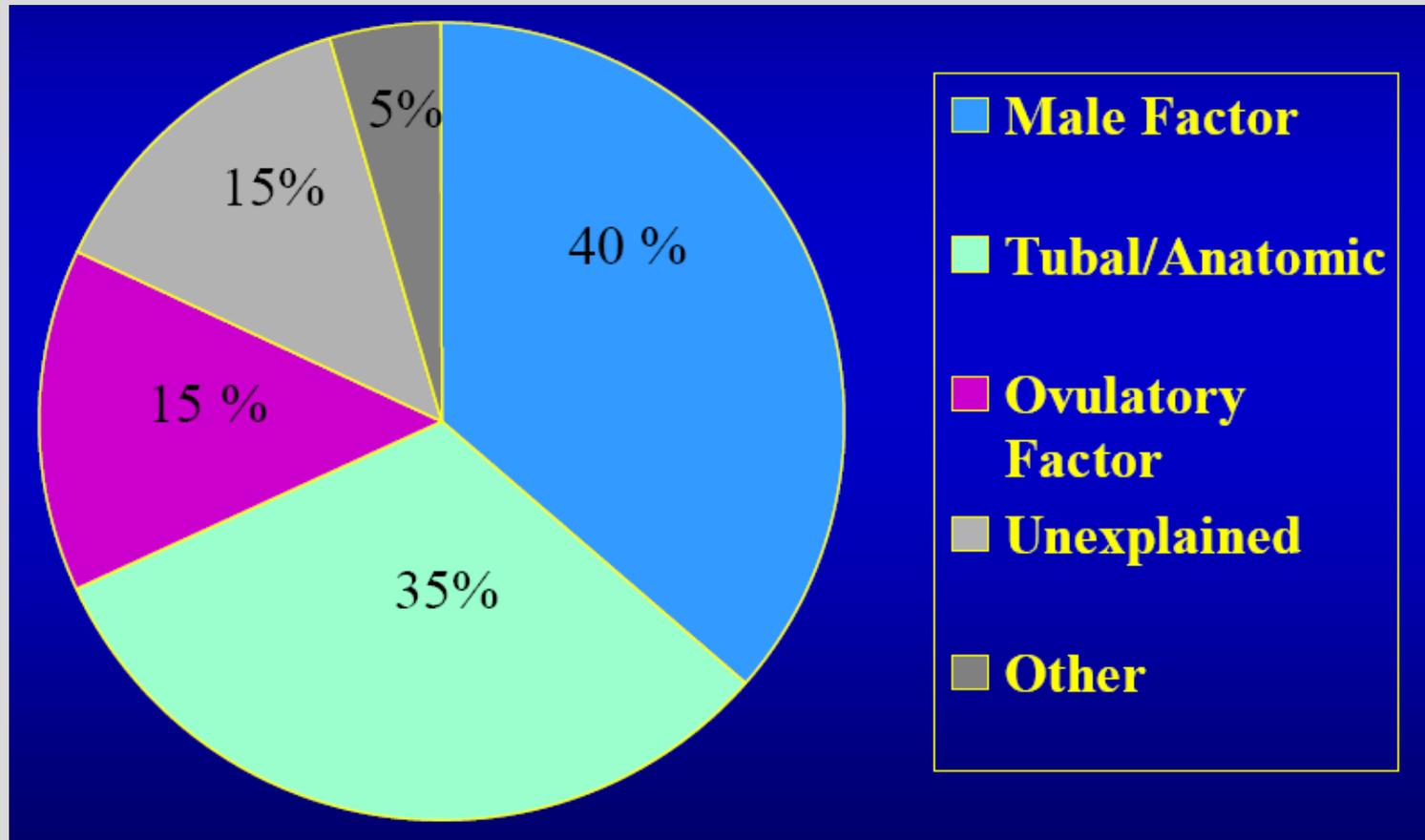
- Clinics and insurance companies define infertility as the inability to achieve pregnancy after one year of unprotected intercourse
- Affects about 8 million reproductive-age couples in the United States (1 in 8), approx. 12% of the reproductive-age population
- Infertility Factoid o' the Day: Which 3 states require all health insurance plans to cover infertility treatments?

Assisted Reproductive Technologies: Methods for Treating Infertility

- **Surgical treatments**
- **Fertility drugs**
- **Intrauterine insemination (IUI)**
- **In vitro fertilization (IVF)**
- **Beyond IVF**

Infertility is an Equal Opportunity Condition

A common misconception is that infertility is primarily a woman's problem—in fact, defects are found in both males and females at similar frequencies.



**Table 2. Risk of Chromosomal Abnormality in Newborns
by Maternal Age**

<i>Maternal Age (years)</i>	<i>Risk for Down Syndrome</i>	<i>Total Risk for Chromosomal Abnormalities</i>
20	1/1,667	1/526
25	1/1,250	1/476
30	1/952	1/385
35	1/378	1/192
40	1/106	1/66
41	1/82	1/53
42	1/63	1/42
43	1/49	1/33
44	1/38	1/26
45	1/30	1/21
46	1/23	1/16
47	1/18	1/13
48	1/14	1/10
49	1/11	1/8

Source: *Maternal Fetal Medicine: Practice and Principles*. Creasy and Resnick, eds. W.B. Saunders, Philadelphia, PA. 1994:71. Reproduced with permission.



"Eureka!"

-- Mike, 1982

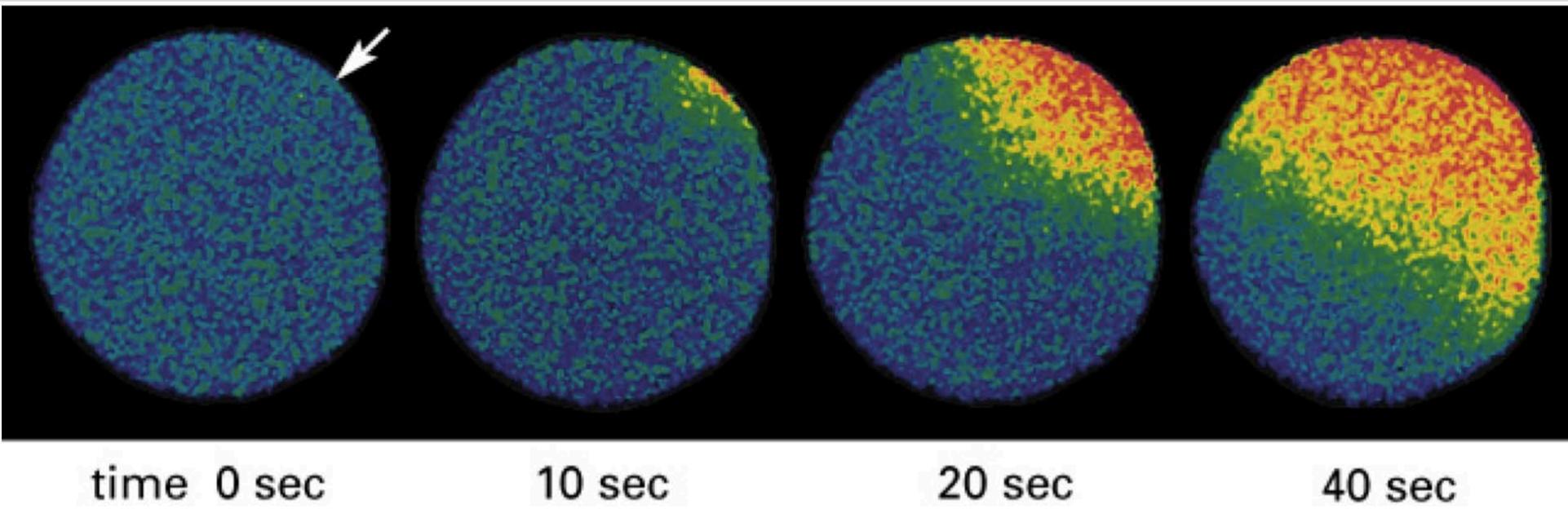
-- Ben, 1984

-- Jenna, 1990

5 μm

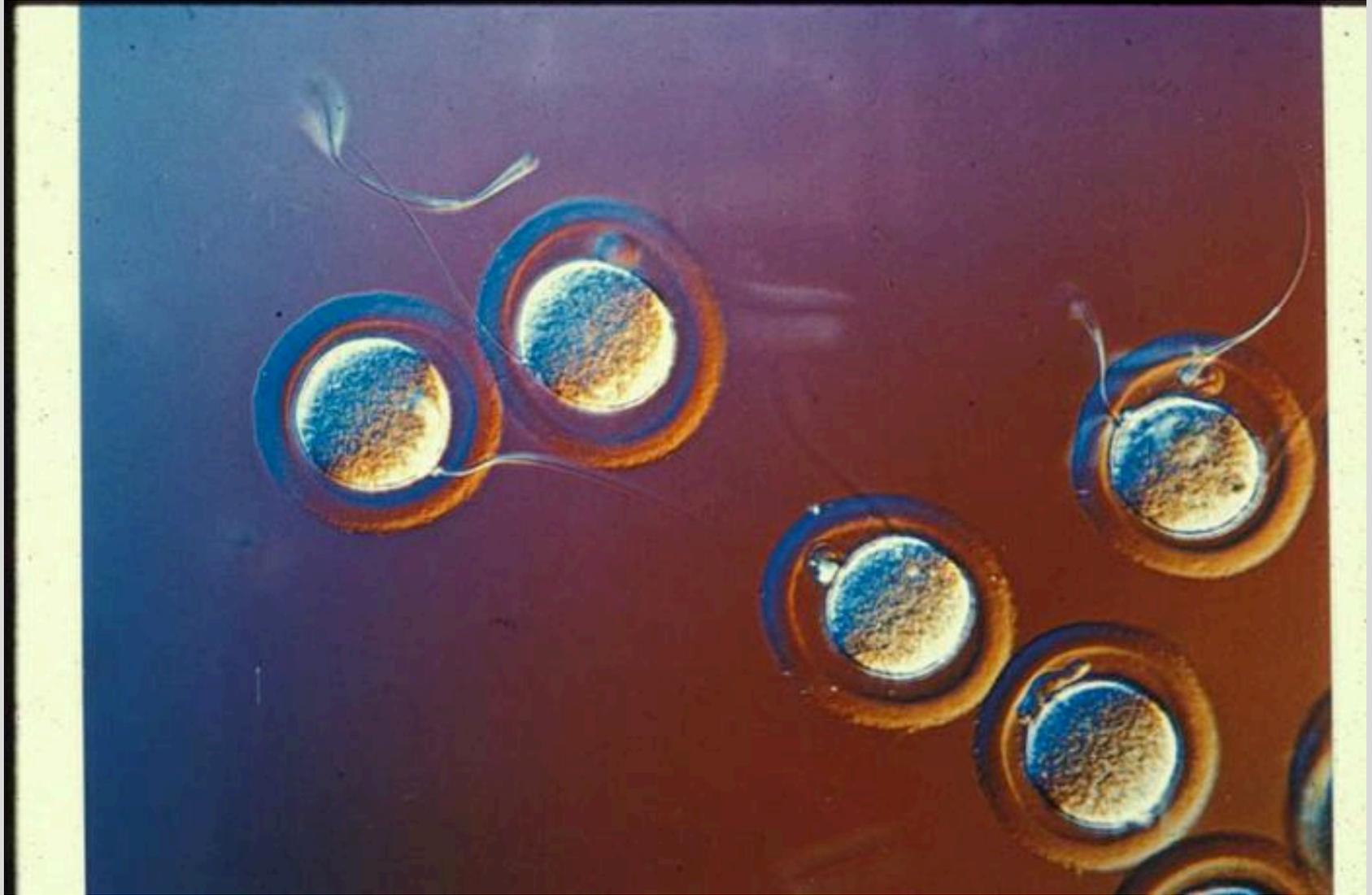
... but only one lucky sperm is chosen.

Fertilization Requires Waves of Cytoplasmic Calcium



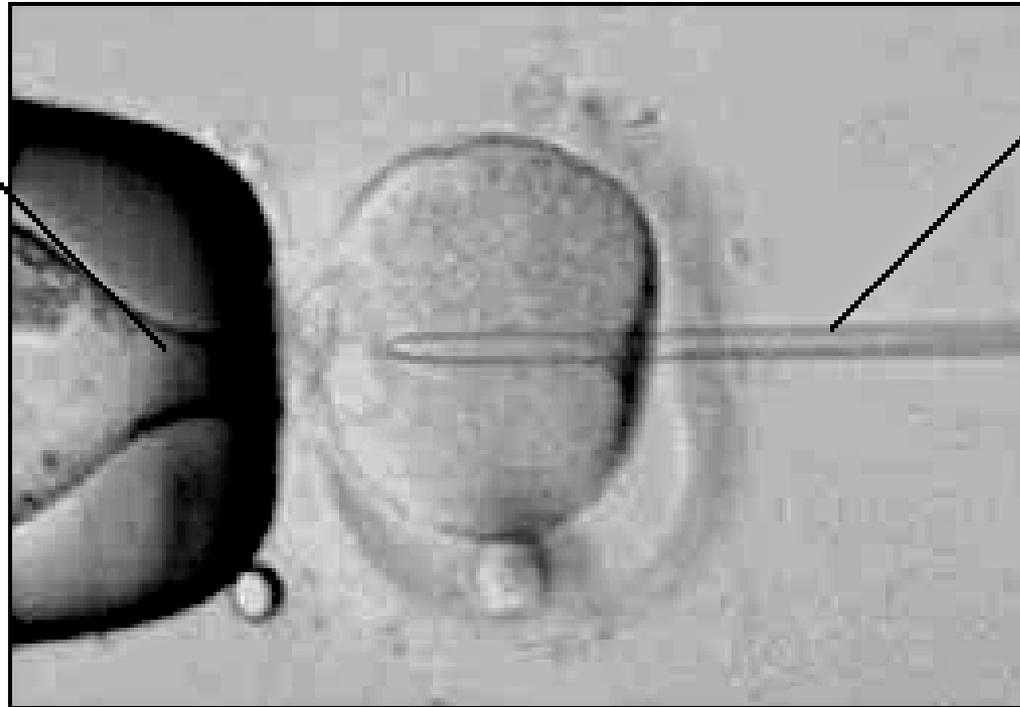
Both the frequency and amplitude of the calcium waves are important for normal development in animal models and in human *in vitro* models

In Vitro Fertilization “Classic”



IVF: Intra-cytoplasmic sperm injection (ICSI)

Larger tube that holds the egg still.



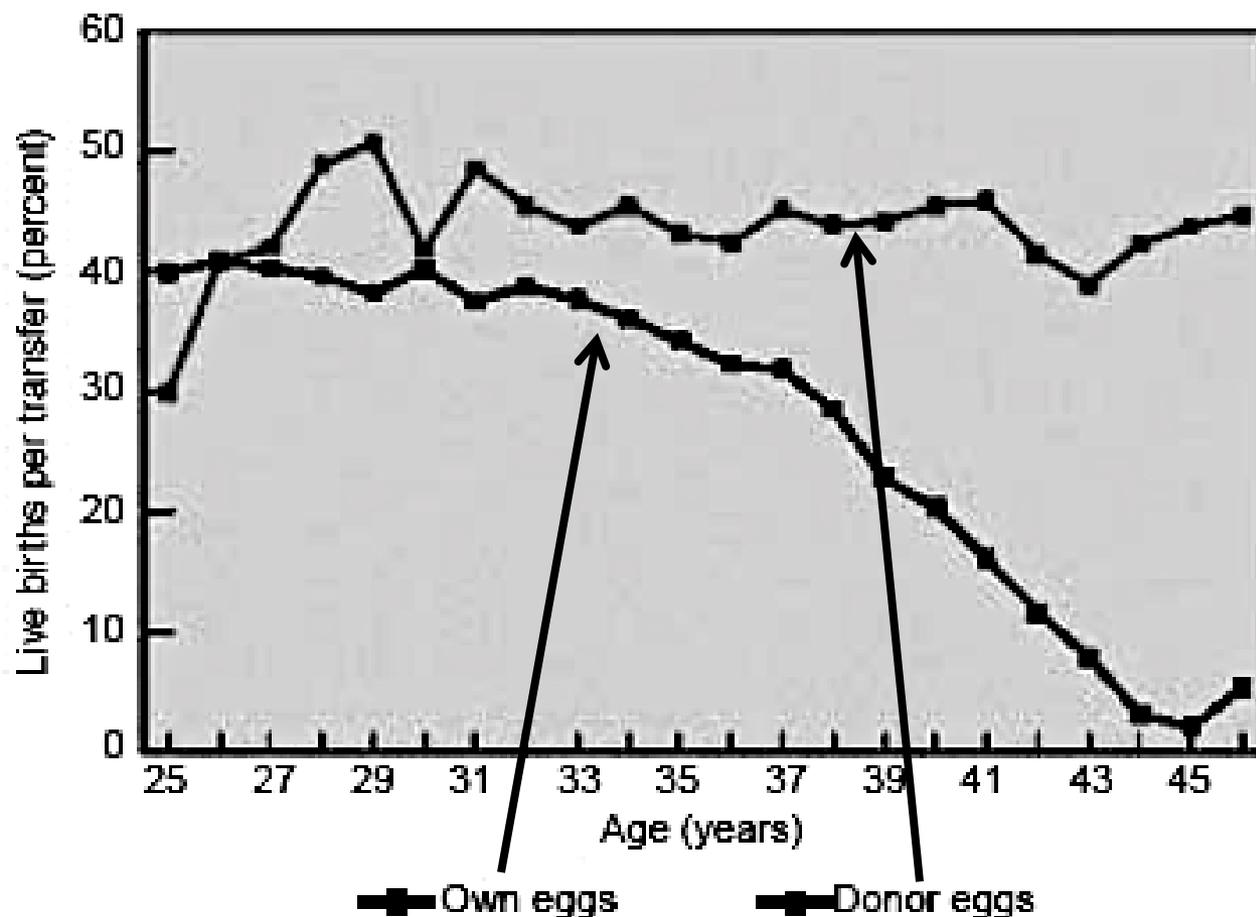
Small glass tube through which the sperm is injected into the egg.

Intracytoplasmic sperm injection (ICSI), in which a sperm is injected directly into an egg to facilitate fertilization.

ICSI of a Human Oocyte



Figure 2. Percentage of Live Births per Transfer for Fresh Embryos From Own and Donor Eggs, by Age of Recipient, 2000



Source: 2000 Assisted Reproductive Technology Success Rates, National Summary and Fertility Clinic Reports. www.cdc.gov/nccdphp/drh/art.htm

Key Point: Success rate of IVF is similar to fertile population until mid-30's

INFERTILITY

IVF Linked to More Birth Defects

By Alexandra Sifferlin | Oct. 22, 2012 | 4 Comments

KAYAK
Just found at KAYAK.com:
Raleigh, NC Hotel Deals

Emerging research is not definitive, but suggests that:

- Infertility itself increases the risk of birth defects
- Congenital birth defects are significantly higher in ICSI babies vs. IVF, IUI, fertility drug, or naturally conceived babies
- Increased risk of obesity, hypertension, and diabetes, especially in ICSI children

Frozen Oocytes: Ready for Prime Time?

- Recall that I told you frozen oocytes would have the greatest effect on reproductive behavior since The Pill . . .
- The American Society for Reproductive Medicine recently decided that the use of frozen oocytes was no longer “experimental”, paving the way for coverage by health insurance companies, a financial boon for IVF clinics . . .
- However, this was based on reviewing take-home baby rates with only 1,000 frozen oocytes under ideal circumstances . . .
- Many leading investigators in the field do not believe frozen oocytes are ready for prime time . . . yet
- Nonetheless, it is clear that this technology will be ready for prime time within the next few years

Full disclosure: I am a member of the ASRM

Ethical Issues



Baby M (Melissa Stern)
Born: March 27, 1986



Mary Beth Whitehead



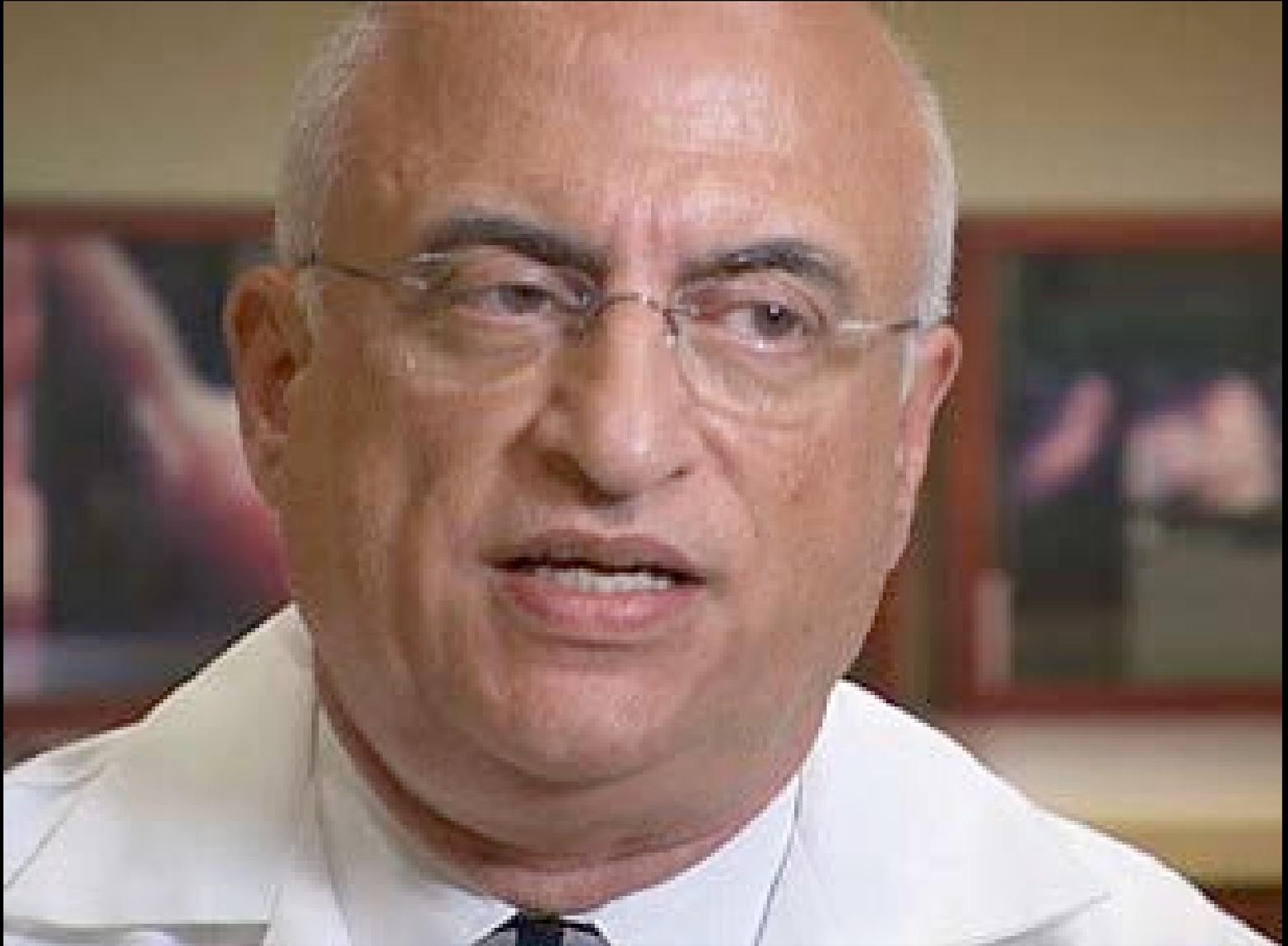
Nadya Suleman
Mother of 14



Noah, Maliyah, Isaiah, Nariyah, Jonah, Josiah, Jeremiah, and Makai

Born: January 26, 2009

Weight range at birth: 1 lb 8 oz (680 g) – 3 lb 4 oz (1,474 g)



Michael Kamrava, MD

Born: January 5, 1940

Gave birth: December 29, 2006

Died: July 11, 2009



Maria Carmen del Bousada



Senator Strom Thurman (66) married Nancy Moore, Miss South Carolina (22)

Controlled Ovarian Hyperstimulation





Sex Selection



Preimplantation Genetic Diagnosis



Designer Babies



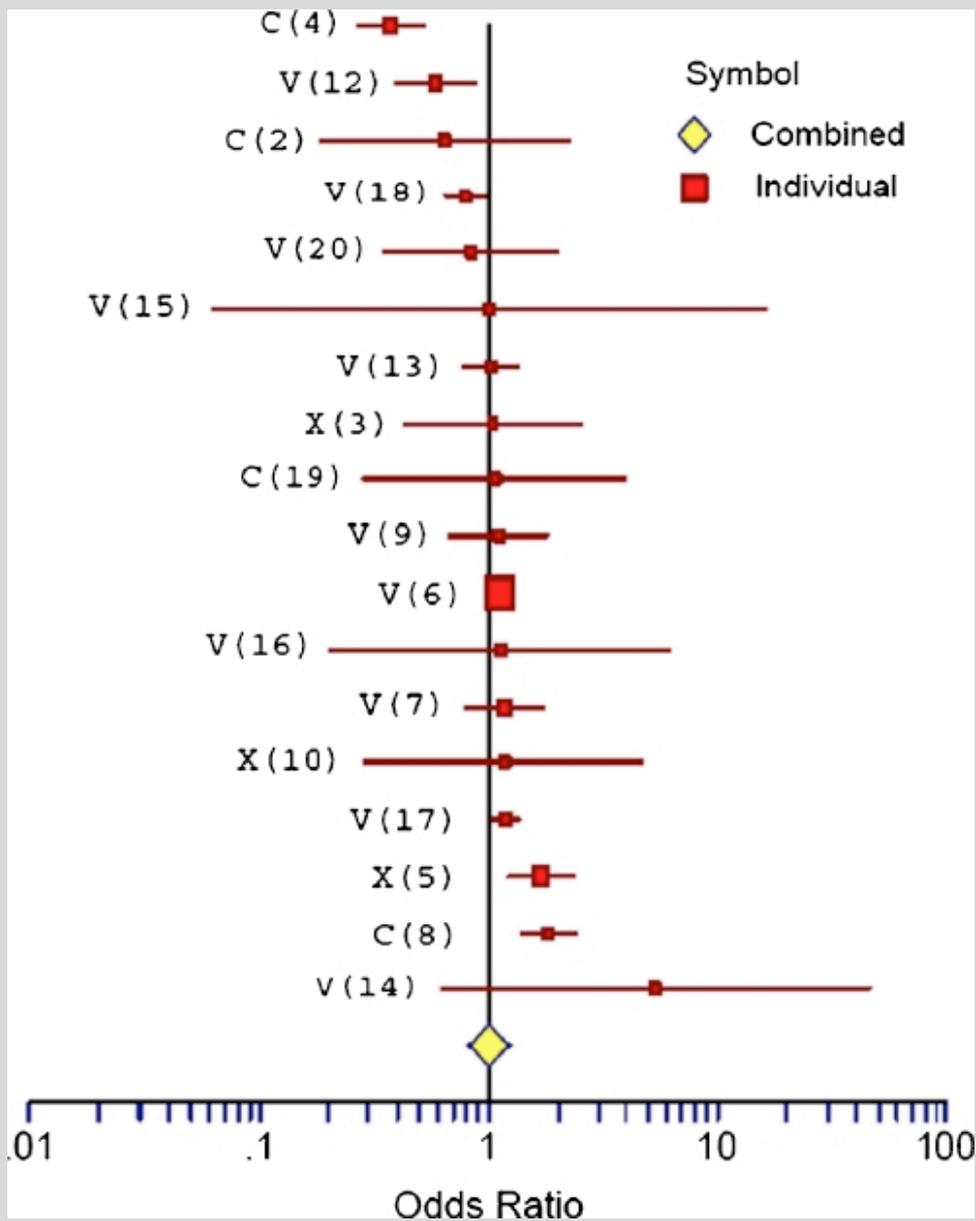
TABLE 3. PREVALENCE OF MAJOR BIRTH DEFECTS DIAGNOSED BY ONE YEAR OF AGE.*

GROUP	NO. OF INFANTS	PREVALENCE	UNADJUSTED ODDS RATIO (95% CI)	ADJUSTED ODDS RATIO (95% CI)†
		no. (%)		
All infants				
Natural conception	4000	168 (4.2)	1.0	1.0
Intracytoplasmic sperm injection	301	26 (8.6)	2.2 (1.3–3.3)	2.0 (1.3–3.2)
In vitro fertilization	837	75 (9.0)	2.6 (1.7–3.0)	2.0 (1.5–2.9)
All singletons				
Natural conception	3906	164 (4.2)	1.0	1.0
Intracytoplasmic sperm injection	186	18 (9.7)	2.4 (1.4–4.1)	2.2 (1.3–3.9)
In vitro fertilization	527	50 (9.5)	2.4 (1.7–3.4)	2.2 (1.5–3.2)
Term singletons‡				
Natural conception	3681	149 (4.0)	1.0	1.0
Intracytoplasmic sperm injection	170	15 (8.8)	2.3 (1.2–4.0)	2.2 (1.2–4.0)
In vitro fertilization	454	38 (8.4)	2.2 (1.5–3.2)	2.1 (1.4–3.2)

*CI denotes confidence interval.

†The odds ratios were adjusted for maternal age and parity, the sex of the infant, and correlation between siblings.

‡Term was defined as at least 37 weeks of gestation.



Forest plot showing the adjusted odds ratios (with confidence intervals) of major malformations for 18 studies comparing IVF and/or ICSI with natural births in subfertile couples.

V: IVF study
 X: ICSI study
 C: Combined results of ICSI and IVF

Rimm A. A meta-analysis of the impact of IVF and ICSI on major malformations after adjusting for the effect of subfertility. *J Assist Reprod Genet.* 28(8):699-705, 2011 Aug

Controversies in ART

- ART is unnatural
- Embryo as a person
- Risks of IVF and ICSI compared to natural conception
- Interests of the child vs. motives of the parents
- Wrongful life?
- A “new eugenics”?
- Commercialization of ART

M'15 Medical Ethics & Professionalism II
Small Group Discussion Cases – Session 3
Student Version

Sex Selection

Mr. and Ms. Carter had been married for 6 years when they visited Dr. Jones, a well-known infertility specialist, to ask for help creating their family. Ms. Carter had given birth to a beautiful, healthy baby girl 3 years earlier. She was the light of their lives, and they loved her dearly. Now that their daughter was in preschool, they had decided it was time for them to complete their family by having another child—a son.

They sat down in the plush chairs in Dr. Jones's office. Mr. Carter spoke first, "We've done a lot of research, Dr. Jones, and we think you can help us. A couple that we are friends with came to you to make sure they had a girl, since they have a disease in their family that runs in boys. We're here to see if you can help us conceive a son for our family."

Dr. Jones was confused about what they were asking for, and why. "Have you been having trouble getting pregnant?" he asked Ms. Carter.

"Oh, no," she responded. "We haven't been trying. We wanted to wait to see you, so that we could make sure we had a boy. We love our daughter, and we always thought it would be perfect to have one of each. A balanced family."

"Hmm," Dr. Jones said. "We have done sex selection for patients in the past, but only based on medical conditions that occur in certain families, like what we did for your friends—"

"No, it's nothing like that," said Mr. Carter. "I just think we should have a boy and a girl. All my life I've envisioned having a kid I can take fishing and play ball with."

"So, what do you think?" Ms. Carter pressed. "Does this sound like something you can help us with?"

American Medical Association Journal of Ethics. February 2012, Volume 14, Number 2: 105-111.

Assisted Reproduction and *Primum Non Nocere*

Mr. and Ms. Concepcion were in many ways not unlike the other couples that had come to the infertility clinic. They were pleasant-appearing, affectionate towards one another, and eager to become parents. They were extremely organized and had brought copies of their relevant medical records. Nevertheless, they managed to capture the attention of the entire waiting room: they both had the characteristic body size and features of [achondroplasia](#) (click for image).

Ms. Concepcion began to rattle off facts in the examining room before Dr. West could even introduce himself. "We understand achondroplasia *very* well. It has autosomal-dominant genetics. When inherited homozygously, it is lethal, but."

"Well, you certainly have done your homework very well," chuckled Dr. West. "I'm Dr. West. How exactly is it that I can help you?"

"We have been trying to become pregnant for years now," chimed in Mr. Concepcion. "We have been to numerous doctors and had every test performed. They finally figured out that I have a slight blockage in the passage of sperm. We were referred to you for in vitro fertilization. Your colleagues say that you're one of the best."

Dr. West went on with a mixture of modesty and pride to describe the clinic's excellent success rates for in vitro fertilization.

Mr. Concepcion then lowered his voice slightly as he elaborated to Dr. West his fears regarding the psychological repercussions on his wife should she conceive a homozygous child who was essentially born only to die. The couple also expressed their strong opposition to abortion. They were simply unwilling to accept a 25 percent chance that their baby would be homozygous for achondroplasia.

"Given what you have just told me," Dr. West asserted, "in conjunction with the complexities of your genetic background, we would consider preimplantation genetic diagnosis to be appropriate in avoiding this outcome and increasing the probability that you would have a child of normal stature."

Mr. and Ms. Concepcion looked shocked. "Well, actually, we were hoping that you might assist us in having a child *with* achondroplasia. How would we care for or understand a child who was not like us?"

Realizing his false assumption, Dr. West thought carefully about his next words. He had never been asked to perform preimplantation genetic diagnosis and specifically choose embryos that would become what many would consider "impaired" children. While medically it may be safe, something didn't sit right with Dr. West.

American Medical Association Journal of Ethics. September 2007, Volume 9, Number 9: 605-610

Procrastinating Parents

Samantha and Benjamin meet in college and fall deeply in love. Sure that she has met the man of her dreams, Sammy decides the wedding will take place as soon as she finishes medical school and Ben returns from his Peace Corp service in Southeast Asia. Unfortunately, things get postponed when Ben takes a interim job in a remote corner of West Africa. As she's finishing a residency in obstetrics and gynecology four years later, Ben decides he can't turn down another

opportunity to work in a rural village deep in the Amazon jungle. Realizing that things aren't working out the way she planned, Sam decides to cryopreserve some of her oocytes for use when and if Ben makes it home.

More than two years go by without another word from Ben. Sam learns from a mutual acquaintance that he had gone to live among the aboriginal inhabitants of an uncharted island in the South Pacific. Resigned to the loss of the love of her life, Sam eventually marries Jack, an anesthesiologist she befriended at one of her training hospitals. She is 36. They have two children (the old fashioned way), move to the suburbs, and get a dog.

Twenty-two years go by. Sam's children are both in college and she continues to work at the same clinic, now serving as its medical director. She is still married, but unhappily. She was never able to accept the fact that she had to settle for the "runner up" husband. One day at work, a nurse tells her there's a man waiting to see her. "He's not a patient. Says he's an old friend."

It was Ben. It turns out he returned from his world travels soon after Sam's first child was born. He had come back intending to marry her, but on hearing this news he abruptly turned around and resumed his work overseas. About a year ago, he was diagnosed with Parkinson's disease. Concluding that this was going to be his last chance, he resolved to "go home" and find Sam.

Two years later, Sam is divorced and living with Ben. They decide to use her cryopreserved oocytes to have a child of their own. They consult Dr. Prego, one of Sam's colleagues, who readily agrees to help. Several rounds of IVF-ICSI (in vitro fertilization with intracytoplasmic sperm injection) and \$60,000 later, Sam gives birth to twin girls at the age of 60.