Genetic Screening in Reproductive Care

Understanding the opportunities and pitfalls of emerging technologies

Ginny Ryan, MD MA (Bioethics)
Assistant Professor, Reproductive Endocrinology and Infertility
Affiliate Faculty, Program in Bioethics and Humanities
University of Iowa Carver College of Medicine
Ethics Consult Service Consultant, University of Iowa Hospitals and Clinics

Objectives

1. Describe current and emerging technologies used for genetic screening in preconception, pre-implantation, and prenatal testing.
2. Identify ethical principles and values that help guide clinicians and patients in the use of genetic screening.
3. Discuss current professional guidelines related to genetic screening in reproductive care.
4. Compare reproductive medicine to other clinical contexts in which genetic testing raises ethical challenges.

Disclosure

I have no relevant financial relationships

with the manufacturer(s) of any commercial product(s) and/or provider(s) of commercial services discussed in this CME activity

Setting the Stage

"The pace at which new information about genetic diseases is being developed and disseminated is astounding.
Thus, the ethical obligations of clinicians start with the need to maintain competence in the face of this evolving science."

Committee on Ethics and Committee on Genetics, American College of Obstetricians and Gynecologists. *Ethical Issues in Genetic Testing* Obstet Gynecol. 2008 Jun;111(6):1495-502. (reaffirmed 2014)

DESCRIBE CURRENT AND EMERGING TECHNOLOGIES

Screening v. Diagnostic Testing

- Screening = strategy used in a population to identify the possible presence of an as-yet-undiagnosed disease in people in good health
  - e.g. mammography
  - designed to identify disease and intervene early to reduce morbidity and mortality
  - in **reproductive genetics**, identifying a mutation in an unaffected parent or a pregnancy marker indicating higher risk of disease in the offspring
- Diagnostic Testing = procedure to detect disease in an individual suspected of having the disease based on symptoms or results of another test
  - e.g. breast biopsy

More Definitions

- **Preconception**
  - Before attempting to become pregnant; sample is: Maternal and paternal serum
  - E.g., a Caucasian couple is asked about family history and tested for CF
- **Pre-implantation**
  - After in vitro fertilization (IVF) and before attempting to implant pre-embryos; sample is: Trophectoderm cells from pre-embryo
  - E.g., a 41 yo woman has her IVF pre-embryos biopsied to decrease her risk of failed treatment cycles
- **Prenatal**
  - During pregnancy; sample is: Maternal serum +/- ultrasound of the fetus
  - E.g., a pregnant woman has integrated screening performed to assess her fetus' risk of Trisomy 21and neural tube defects
- **Newborn**
  - In first days after birth; sample is: Newborn serum
  - E.g., opt out testing is performed from a heel stick to screen for 50 heritable disorders

University of Iowa Carver College of Medicine

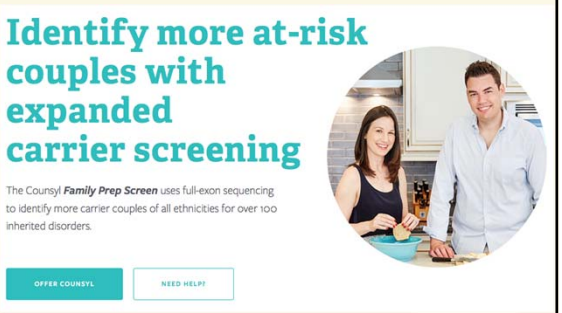
Preconception Screening Options

Universal counseling and focused vs. universal testing of genetic parents

- Goal: lower risk for, or avoid, disease in a child, prepare for child with disease (or pre-disease)
- Based on personal or family history of disease
  - Issues of limited knowledge and family impact
- Based on race / ethnicity
  - Increasing understanding of pan-ethnic nature of the population
- When to involve genetic counselors
  - Complexity, availability, cost
  - Pre- and post-test

University of Iowa Carver College of Medicine

Private Companies Market Low Cost Screening



https://www.counsyl.com

Private Companies Market Low Cost Screening

Firm Brings Gene Tests to Masses

By ANDREW POLLACK
Published: January 28, 2010
REDWOOD CITY, Calif. — The new movie "Extraordinary Measures" is based on the true story of a father who starts a company to develop a treatment for the rare genetic disease threatening to kill two of his children before they turn 10. Now, a Silicon Valley start-up is making the bold claim that it can help eradicate that disease and more than 100 others by alerting parents-to-be who have the carrier genes.

https://www.counsyl.com/about/press/
http://www.nytimes.com/2010/01/29/business/29gene.html

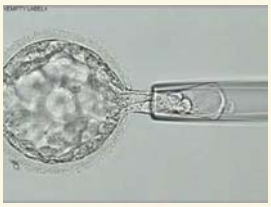
Pre-implantation Screening Options

- Goal: avoid miscarriage and disease in child
- Screening is different from pre-implantation genetic diagnosis
- Clinical indications and use in practice
  - Age
  - Recurrent pregnancy loss, recurrent IVF treatment failure
- BUT, concern for overuse, inflation of IVF results and marketing

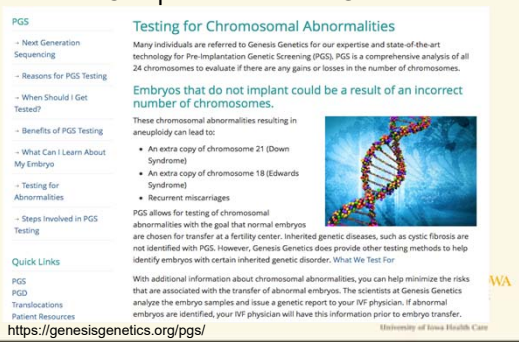
University of Iowa Carver College of Medicine

Pre-implantation Screening Details

Below: photo from UIHC of trophectoderm biopsy



Private Companies Market PGS Benefits


PGS
→ Next Generation Sequencing
→ Reasons for PGS Testing
→ When Should I Get Tested?
→ Benefits of PGS Testing
→ What Can I Learn About My Embryo
→ Testing for Abnormalities
→ Steps Involved in PGS Testing
Quick Links
PGS
PGD
Translocations
Patient Resources

Testing for Chromosomal Abnormalities

Many individuals are referred to Genesis Genetics for our expertise and state-of-the-art technology for Pre-Implantation Genetic Screening (PGS). PGS is a comprehensive analysis of all 24 chromosomes to evaluate if there are any gains or losses in the number of chromosomes.

Embryos that do not implant could be a result of an incorrect number of chromosomes.

These chromosomal abnormalities resulting in aneuploidy can lead to:

- An extra copy of chromosome 21 (Down Syndrome)
- An extra copy of chromosome 18 (Edwards Syndrome)
- Recurrent miscarriages

PGS allows for testing of chromosomal abnormalities with the goal that normal embryos are chosen for transfer at a fertility center. Inherited genetic diseases, such as cystic fibrosis are not identified with PGS. However, Genesis Genetics does provide other testing methods to help identify embryos with certain inherited genetic disorder. What We Test For

With additional information about chromosomal abnormalities, you can help minimize the risks that are associated with the transfer of abnormal embryos. The scientists at Genesis Genetics analyze the embryo samples and issue a genetic report to your IVF physician. If abnormal embryos are identified, your IVF physician will have this information prior to embryo transfer.

University of Iowa Health Care

https://genesisgenetics.org/pgs/

Prenatal Screening Options

- Goal: avoid or prepare for disease in child
- Established
  - 1st trimester screening
  - Integrated screening
  - Statewide programs established
- Emerging
  - Non-invasive prenatal diagnosis via cell-free fetal DNA
  - Screening vs. diagnosis
  - Private companies and increased direct to consumer marketing

University of Iowa Carver College of Medicine
University of Iowa Health Care

Private Companies Market CFFDNA

About the Test

The MaterniT21 PLUS test, developed and validated by Sequenom CMM, is a laboratory-developed test (LDT) that analyzes circulating cell-free DNA extracted from a maternal blood sample. The test detects the relative amount of 21, 18, 13 and Y chromosomal material.[2, 10]

http://www.sequenomcmm.com/Home/Health-Care-Professionals/Trisomy-21/About-the-Test

Use at UIHC:

- AMA (Advanced Maternal Age)
- Abnormal serum screening
- Abnormal ultrasound
- Family history of genetic abnormalities

IDENTIFY ETHICAL PRINCIPLES AND VALUES

University of Iowa Carver College of Medicine
University of Iowa Health Care

Ethics of Screening Programs

- Respond to a recognized need
- Define objectives at the outset
- Define target population
- Base on scientific evidence of effectiveness
- Integrate education, testing, clinical services and program management
- Ensure quality assurance to minimize potential risks
- Ensure informed choice, confidentiality and respect for autonomy
- Promote equity and access for the entire target population
- Plan program evaluation from the outset
- Ensure overall benefits of screening outweigh the harm

From: Anne Andermann, Ingeborg Blancquaert, Sylvie Beauchamp, Véronique Déry Revisiting Wilson and Jungner in the genomic age: a review of screening criteria over the past 40 years: Bulletin of the World Health Organization; 2008 Volume 86, Number 4, April 2008, 241-320 http://www.who.int/bulletin/volumes/86/4/07-050112/en/

University of Iowa Carver College of Medicine
University of Iowa Health Care

Unique Ethical Issues in Genetics

- Genetic exceptionalism
  - Genetic information is unique and should be treated differently from other medical information
- Genetic reductionism / determinism
  - Genes determine how an organism turns out
- Technologic imperative
  - New technologies are inevitable, essential and must be developed and accepted for the good of society
- Eugenics
  - Set of beliefs and practices aimed at improving the genetic quality of the human race

University of Iowa Carver College of Medicine
University of Iowa Health Care

Principlist Approach

- Autonomy and right to know / not to know
  - self-determination free from controlling interferences by others and personal limitations preventing meaningful choice
  - Individual AND family, now AND in future
  - Responsibility of provider to provide non-directive counseling and understand and apply testing appropriately, OR refer
- Beneficence and non-maleficence
  - Are we moving towards an expectation of perfection?
- Justice
  - Testing is expensive
  - Testing and treatment is not offered or available to all
- Direct to Consumer Marketing problematic

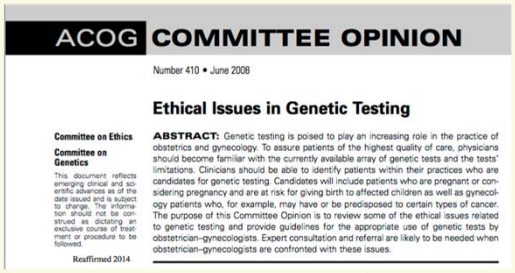
DISCUSS CURRENT PROFESSIONAL GUIDELINES

ACOG Practice Bulletins and Committee Opinions in conjunction with ACMG and SMFM

- "Ethical Issues in Genetic Testing" (CO #410)
- "Screening for Fetal Aneuploidy" (Practice Bulletin #163, May 2016)
- "Prenatal Diagnostic Testing for Genetic Disorders" (Practice Bulletin #162, May 2016
- "Cell-free DNA Screening for Fetal Aneuploidy" (CO #640)

ASRM Ethics Committee Documents

- "Moving Innovation to Practice" (2015)
- "Use of Preimplantation Genetic Diagnosis for Serious Adult-Onset Conditions" (2013)



ACOG COMMITTEE OPINION

Number 410 • June 2008

Ethical Issues in Genetic Testing

Committee on Ethics

Committee on Genetics

This document reflects emerging clinical and scientific advances as of the date issued and is subject to change. The information should not be construed as dictating an exclusive course of treatment or procedure to be followed.

Reaffirmed 2014

ABSTRACT: Genetic testing is poised to play an increasing role in the practice of obstetrics and gynecology. To assure patients of the highest quality of care, physicians should become familiar with the currently available array of genetic tests and the tests' limitations. Clinicians should be able to identify patients within their practices who are candidates for genetic testing. Candidates will include patients who are pregnant or considering pregnancy and are at risk for giving birth to affected children as well as gynecology patients who, for example, may have or be predisposed to certain types of cancer. The purpose of this Committee Opinion is to review some of the ethical issues related to genetic testing and provide guidelines for the appropriate use of genetic tests by obstetrician–gynecologists. Expert consultation and referral are likely to be needed when obstetrician–gynecologists are confronted with these issues.

COMPARE TO OTHER CONTEXTS

- Pediatrics
  - Newborn screening – Iowa law mandates testing for 50 inherited disorders
- Biobanks / cord blood banks
  - Benefit to science vs. participant
  - Consumer marketing
  - Hybrid
- Personalized medicine
  - Genomics for individualized treatment
  - E.g., breast cancer


www.wiringthebrain.com

Genetic information:
- Is increasingly available, but not to all
- Is imperfect
- Offers opportunity and expectation

Healthcare providers must:
- Keep abreast of state of the science
- Understand the limitations of the tests and their own knowledge
- Always keep the patient's goals in mind

Ginny Ryan
319-384-9170
Ginny-ryan@uiowa.edu

UNIVERSITY OF IOWA CARVER COLLEGE OF MEDICINE
University of Iowa Health Care