

1. Legal and Ethical Issues in Human Genetics

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2. Confidentiality

Confidentiality

- ◆ Physicians are required by law to hold what they learn from their patients in confidence.
- ◆ BUT genetic information is FAMILY-CENTERED by nature
- ◆ When is it ok to breach confidentiality?

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3. Malpractice Law

Malpractice Law

- ◆ Failure to alert patients about relevant genetic tests may lead to wrongful birth lawsuits.
- ◆ Down Syndrome and amniocentesis
- ◆ Neural tube defect and alpha-fetal protein
- ◆ Canavan screening in Ashkenazi Jewish
- ◆ Cystic Fibrosis screening offered to all couples considering a pregnancy

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4. Genetic Discrimination

Genetic Discrimination

- ◆ Concern that genetic information will be used to deny or limit access to insurance and employment.
- ◆ Federal (HIPPA) and state laws in place to provide protection for patients in group health plans.
- ◆ Current laws do not address discrimination by Life Insurance Companies

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5. Genetic Discrimination

Genetic Discrimination

- ◆ EEOC issued a guideline in 1995 interpreting the American with Disabilities Act as forbidding employers from using genetic information in hiring or promotion.
- ◆ Despite widespread fears, there is little evidence that predictive genetic information has yet been used to deny health insurance or employment.

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6. Regulation of Human Genome Research

Regulation of Human Genome Research

- ◆ Intellectual Property: who owns the tissue samples: patient vs. laboratory
- ◆ To whom does “The Human Genome” belong?
 - **Individuals**
 - **Family**
 - **Society**

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7. Gene Patents

Gene Patents

- ◆ The creation of intellectual property based on DNA sequence information
- ◆ Patents on human genes ‘offend the principle of the sanctity of human life’
- ◆ Biotechnology industry: patent protection is “an essential element of the commercialization process”.

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8. Ethical Challenges in Genetic Testing

Ethical Challenges in Genetic Testing

- ◆ Rapid advances in genetic technology and the Human Genome Project are predicted to revolutionize current medical practice.
- ◆ Are physicians/geneticists ordering genetic tests aware of the relevant ethical principles and legal obligations resulting from this new technology?

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9. Views on Genetic Testing

Views on Genetic Testing

**I feel comfortable with my knowledge
of available genetic tests** **18 %**

**I have a standard for deciding when
patients need to be informed about
the option of genetic testing** **28 %**

**I am comfortable counseling patients
before and after genetic testing** **17 %**

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10. Autonomy

Autonomy

- ◆ Patients facing choices regarding genetic testing are entitled to exercise personal autonomy free from undue pressures and equipped with adequate information to understand the implications for themselves and others of the available options.

• B Dickens, 1996

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11. Beneficence / Nonmaleficence

Beneficence / Nonmaleficence

- ♦ **Beneficence**: The duty to do and to maximize good
- ♦ **Nonmaleficence**: the duty to do no harm or to minimize harm in pursuing a greater good

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12. Legal Responsibilities of Health Care Providers

Legal Responsibilities of Health Care Providers

- ♦ **Patient-physician confidentiality ensures maintenance of privacy for the patient**
- ♦ **Known exceptions to the protection of confidentiality of medical information:**
 - Tarasoff case (1976)-threat of violence

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13. Case 3: Familial Adenomatous Polyposis

Case 3: Familial Adenomatous Polyposis

- ◆ RM is a 47 year old man has been diagnosed with FAP and colon cancer. He undergoes colectomy.
- ◆ RM has 6 children aged 4-25. He and his family are referred for genetic counseling.

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14. Familial Adenomatous Polyposis

Familial Adenomatous Polyposis

- ◆ 1% of colon cancer
- ◆ Incidence 1/10,000
- ◆ >100 polyps develop diffusely throughout the colon
- ◆ 50% of patients develop adenomas by age 15
- ◆ 100% of patients develop cancer by age 40

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15. Genetic testing for FAP

Genetic testing for FAP

- ◆ Gene Sequencing: **90%** sensitive
- ◆ Aggressive gene testing in at-risk individuals
- ◆ TEST MINORS
- ◆ Aggressive colonic screening beginning at puberty
- ◆ Colectomy recommended for affected pts

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16. Case 3: Familial Adenomatous Polyposis

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- ◆ RM is a 47 year old man has been diagnosed with FAP and colon cancer. He undergoes colectomy.
- ◆ RM has 6 children aged 4-25. He and his family are referred for genetic counseling.
- ◆ **He cancels the first appointment and 'no shows' the second. The third appt he came to the hospital, but then left the parking lot before entering the building.**

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17. Ethical Principles of Concern:

Ethical Principles of Concern:

- ◆ Privacy (patient)
- ◆ Duty to warn (children)
- ◆ Right not to know

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18. Duty to Warn Third Parties Safer v. Pack (1996)

*Duty to Warn Third Parties
Safer v. Pack (1996)*

- ◆ In 1954 a man dies at age 45 of complications of colon cancer. He has two daughters, ages 17 and 10.
- ◆ Twenty-six years later (1980), the younger daughter is diagnosed with metastatic colon carcinoma and Familial Adenomatous Polyposis.

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19. Duty to Warn Third Parties Safer v. Pack (1996)

Duty to Warn Third Parties Safer v. Pack (1996)

- ◆ She obtains her father's medical records and learns that he also was diagnosed with Familial Adenomatous Polyposis.
- ◆ She sues her father's doctor's estate (Dr. Pack died in 1969) for 'violation of a duty to warn, failing to inform her of a foreseeable, avoidable risk'.

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20. Duty to warn third parties, cont.

Duty to warn third parties, cont.

- ◆ She alleged that
 - FAP invariably leads to colon cancer
 - Dr. Pack knew of the hereditary nature of her father's illness
 - Dr. Pack was 'required by the standards prevailing at the time to warn individuals at risk so that they could seek early exam, detection and treatment'.

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21. Duty to warn third parties, cont.

Duty to warn third parties, cont.

- ◆ Trial court dismissed the claim on the grounds that Dr. Pack had no legal duty to warn a patient's child of a genetic risk
- ◆ Unlike contagious risk, or risk of harm, genetic risk was already present within the child
- ◆ the child did not have a patient-physician relationship with Dr. Pack

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22. Duty to warn third parties, cont.

Duty to warn third parties, cont.

- ◆ In appeal, the superior court of NJ reversed the lower court's decision
 - lower court erred in determining that the disease was unavoidable and unforeseeable
 - genetically transmissible condition is sufficiently similar to a contagious disease
 - individual is easily identified
 - substantial future harm may be averted or minimized by a timely and effective warning

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23. Ethical Issues to Consider:

Ethical Issues to Consider:

- ◆ Patient confidentiality (was her father unaware of genetic implications of his illness or did he choose not to tell them?)
- ◆ Duty to warn...can physicians get in trouble for breaching patient confidentiality?
- ◆ ASHG is calling for 'legal privilege' for physicians: to be given a discretionary right to disclose genetic info to at-risk relatives without incurring liability

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24. Genetic Testing in Minors

Genetic Testing in Minors

- ◆ Carrier testing: wait until the child is old enough to decide for him/herself if knowledge of carrier testing is desired (privacy, non-maleficence)
- ◆ Pre-dispositional testing: consider testing if a **defined medical benefit** can be seen during childhood (beneficence)
 - retinoblastoma, FAP, VHL: childhood tumors can be screened for, improving survival

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25.

Genetic Testing in Minors

Genetic Testing in Minors

- ◆ Pre-symptomatic testing for late onset diseases: wait until child is old enough to decide for him/herself if knowledge of genetic status is desired. (privacy, non-maleficence)
- ◆ Pre-symptomatic testing for childhood onset diseases: ???

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26.

Friedreich Ataxia Case 1

Friedreich Ataxia Case 1

- ◆ JJ is a 9 year old boy who presents with tremors and unsteady gait.
- ◆ FRDA testing reveals two expanded alleles, confirming the diagnosis of Friedreich Ataxia (FA).
- ◆ FA is an Aut. Recessive progressive neurological disorder where pts are usually wheelchair bound by about age 18.

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27.

Freidreich Ataxia Case

Freidreich Ataxia Case

- ♦ JJ has 4 younger siblings between the ages of 8 years and 22 months.
- ♦ Parents want pre-symptomatic testing for the younger siblings.
- ♦ What are the pros and cons of testing the siblings at this time?

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Issues to consider:

Issues to consider:

- ♦ What are the rights of the children? Can parents speak for them?
- ♦ Is there any point to doing testing if this is an untreatable condition?
- ♦ Do you have to order a genetic test just because parents request it?
- ♦ Are you worried that pre-symptomatic children will be treated differently by the parents than unaffected children?

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29. Case: Hemophilia in the family?

Case: Hemophilia in the family?

- ♦ A 30 year old woman, AP, is shown by direct DNA testing to be a carrier of severe Factor VIII deficiency after losing her newborn son to an intracranial hemorrhage.
- ♦ AP has 2 younger sisters and one healthy brother. Their mother who died of alcohol-related liver disease was adopted and they had no further information re:family history.

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30. Case: Hemophilia in the family?

Case: Hemophilia in the family?

- ♦ After discussing X-linked inheritance, recurrence risk and options for future pregnancies, you bring up the potential risk of either or both of AP's sisters being carriers for hemophilia.
- ♦ AP is adamant that she hasn't communicated with her sisters in 8 years and wasn't about to start now, hemophilia or no!

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31. Ethical Principles to Consider:

Ethical Principles to Consider:

- ◆ Privacy of AP's genetic information
- ◆ Duty to disclose to family members

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32. Case 1: CF Newborn Screening

Case 1: CF Newborn Screening

- ◆ 2/99: Mass. pilot program for CF newborn screening
- ◆ 'opt out design'
- ◆ top 5% of daily IRT (immunoreactive trypsinogen) samples are screened for common mutations
- ◆ predicted to detect >98% of affected patients and 'some' carriers as well

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33.

Case 1: CF Newborn Screen

Case 1: CF Newborn Screen

- ◆ HJ is a healthy newborn found to have elevated IRT on newborn screen
- ◆ Mutation analysis reveals one $\Delta F508$
- ◆ Sweat test is negative, indicating HJ is a carrier
- ◆ Parents are seen in clinic, genetic counseling is provided, mutation analysis offered

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34.

Case 1: CF Newborn Screening

Case 1: CF Newborn Screening

Reasons to offer mutation analysis to parents:

- to see if both are carriers (future reproductive decisions)
- to provide info to other relatives

**Result: NEITHER PARENT IS A CARRIER
OF THE $\Delta F508$ MUTATION!!**

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35. Possible Explanations for Discrepancy:

Possible Explanations for Discrepancy:

1. Lab Reporting Error
2. Newborn Screen sample mix-up
3. Parental Sample mix-up
4. Baby is a new mutation for dF508
5. Non-paternity
6. Baby switch at birth

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36. How to proceed?

How to proceed...

1. Have the newborn screen and commercial lab re-run existing samples to check for reporting error
2. Ask for repeat samples from baby and parents to rule out sample mix-up
3. Ask the mother confidentially about the possibility of non-paternity
4. Offer the parents further DNA testing to differentiate between new mutation vs. non-paternity vs. baby switching

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37. Ethical Principles of Concern:

Ethical Principles of Concern:

1. Duty to disclose vs. nonmaleficence:
unsuspected paternity?
2. Autonomy/privacy: Can results be given to
each parent privately or need it be done in
context of family (as it was ordered) ?

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38. Case: Known but unknowing patients with Factor V Leiden Defic...

*Case: Known but unknowing
patients with Factor V Leiden
Deficiency*

- ◆ Clinical molecular biologist calls for advice regarding 3 patients whose DNA he had been sent for CF carrier mutation analysis.
- ◆ Two years later, he used those samples (among others) to help design an assay for the common clotting disorder, Factor V Leiden deficiency.

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39. Case: Known but unknowing patients with Factor V Leiden Defic...

*Case: Known but unknowing
patients with Factor V Leiden
Deficiency*

- ◆ He discovered, serendipitously, that these 3 patients carried the mutation and thus were at significant risk, compared to the general population, for clotting episodes.
- ◆ He asks your advice on how to proceed.... Should he... or you... inform the patients of the results of a test to which they did not consent?

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40. Ethical Principles to consider:

Ethical Principles to consider:

- ◆ Privacy / autonomy of patients: right not to know
- ◆ Duty to disclose: prophylactic treatment is sometimes used in Factor V Leiden deficiency and can be life-saving

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41. Case 2: 14 year old female with lack of pubertal development...

*Case 2: 14 year old female with
lack of pubertal development*

- ◆ JJ was born the 6 pound product of an uncomplicated pregnancy.
- ◆ Puffy feet were noted at birth
- ◆ JJ had normal growth (height 50%) and normal development

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42. Past Medical History

Past Medical History

- ◆ Supraventricular tachycardia and bicuspid aortic valve
- ◆ hernia repair age 2
- ◆ appendectomy age 11
- ◆ ear tubes placed x3
- ◆ healthy sister, maternal half sister and maternal half brother

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43.

Physical Exam

Physical Exam

- ◆ Height 50%; Weight 75%
- ◆ Non-dysmorphic face
- ◆ Ears: borderline low-set
- ◆ Neck, chest, heart, abdomen, back, neuro: unremarkable
- ◆ Ext. exam negative for cubitus valgus or short metacarpals

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44.

Physical Exam, cont.

Physical Exam, cont.

- ◆ Residual puffiness over proximal phalanx of all toes
- ◆ Genitalia: unambiguous female with Tanner I breast and no pubic or axillary hair

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45.

Work-up:

Work-up:

Chromosomes

Labs:

Thyroid-normal	Testosterone-low
LH-high	Estradiol-low
FSH-very high	DHEAS-normal

Pelvic Ultrasound:

Prepubertal uterus. No ovaries identified.

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46.

Follow-up

Follow-up

- ♦ What do you tell parents and patient about XY karyotype?
- ♦ If you leave out the part about the 'Y' chromosome, are they likely to hear it from someone else?
- ♦ Can you tell the patient and family that she has a form of Turner Syndrome and leave it at that?

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47.

Ethical Principles of Concern:

Ethical Principles of Concern:

- ◆ Nonmaleficence
- ◆ Autonomy

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