Ethical Issues in Clinical Cancer Genetics

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OUTLINE

- Privacy Issues
- Duty to Warn
- Justice: Access to medical care
- Testing minors
- Pharmacogenetics & Secondary Information
“Will we have the WISDOM to use this valuable information in ways that will be HELPFULL rather than HARMFULL?”

David J. Doukas

Doukas, J Clin Ethics 2:258-259

Privacy in Clinical Cancer Genetics
Privacy & Genetic Testing

“others should not have a claim to another person’s genetic information unless the patient explicitly consents to the release of this information”*

From the Cancer Genetics Studies Consortium Consensus Statement

*Doukas DJ, Berg JW. Amer J Bioethics 1:2-10, 2001

Privacy in Patient Records

- Should genetic test results be part of the medical record?
  - Shared with other treating physicians

- Is genetic information more sensitive than other medical information, requiring more security?
OPTIONS

- Record genetic information in patient charts
  - providing confidentiality that is equal to other medical information
  - poses an insurance risk to patients

- Keep genetic data in separate charts

Privacy v. family responsibility

- Physician has an obligation to respect the patient’s autonomy and privacy desires
- BUT...
  - Third parties may have competing ethical claims that are relevant
  - Family members have some ethical responsibility to other blood relatives

Doukas DJ, Berg JW. Amer J Bioethics 1:2-10, 2001
Duty to Warn

“A key assumption underlying the ethical justification for a “duty to warn” is the availability of medical interventions to reduce the risk of developing a disease or to lessen the ensuing harm.”

Tarasoff Case (1976)

- Psycotherapist was found at fault for not warning a female victim of the patient’s stated intention to kill her
- “serious and imminent threat”

- Is a probability for cancer a “serious and imminent threat?”

HIPPA

- Protects patients from the disclosure of “individually identifiable information”

- EXCEPTION:
  - Imminent and serious threat AND
  - Physician has the capability of averting significant harm
Professional Guidelines

- Professional duty to warn is discretionary and not compulsory

- “genetic Miranda Warning” from the AMA

- ASCO: cancer care providers’ obligation is fulfilled by informing the patient undergoing testing of the risk to family members

Case Law & Duty to Warn

- **Schroeder v. Perkel** (1981)
  - Physician’s professional duty may extend beyond the patient

- **Pate v. Threlkel** (1995)
  - Doctor’s responsibility is fulfilled with warning the patient of the risk to family members

- **Safer v. Estate of Pack** (1996)
  - Doctor must take “reasonable steps” to guarantee that immediate family members are warned
Informing by letter

- **Control Group**: carriers were asked to inform their at-risk individuals
- **Intervention Group**: letter was sent to at-risk individuals
- Genetic status clarified in 40% in intervention group compared to 23% (P=0.001)

☆ None of the relatives in the intervention group expressed concern for a breach of privacy or autonomy

Justice
Justice: Access to Care

Will my insurance cover a prophylactic mastectomy if I am positive for a BRCA mutation?

Genetic Testing of Minors
Genetic testing of minors

I want my daughter to take the BRCA test.

The ethical dilemma:

Should genetic testing for \textit{BRCA1} & \textit{BRCA2} be offered to minors?

Genetic testing of asymptomatic minors for adult-onset disease
Guidelines for the genetic testing of children

- International Huntington Assoc/World Federation of Neurology (1990)
  “if medical and psychological benefits of a genetic test will not accrue until adulthood, as in the case of adult-onset diseases, genetic testing should generally be deferred”
- NSGC (1995)
  With counseling and caution, parents may be able to make genetic testing decisions for children
- ASCO (2003)
  Cancer genetics professional should be an advocate for the best interests of the child

Legally not prohibited with parental consent and minor assent

Arguments for and against testing minors

**PROS**
- Autonomy of the minor
- Psychological benefits
- Parents know best
- Planning for the future

**CONS**
- Future autonomy
- Negative psychological consequences
- Justified beneficence
- “Limited horizons”
- Confidentiality
When is the appropriate time?

🌟 No empiric data to support either position

Minimal adverse psychological consequences
Promotes effective preventive behaviors

Do you think children under the age of 18 should be given the opportunity to be tested?

n= 42

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<tr>
<td>NO</td>
<td>27</td>
<td>64%</td>
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<tr>
<td>YES</td>
<td>13</td>
<td>31%</td>
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<tr>
<td>Not sure</td>
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Those opposed to genetic testing of minors: Why?

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<tr>
<th>Reason</th>
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<tr>
<td>No medical indication</td>
<td>14</td>
<td>52%</td>
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<tr>
<td>Potential negative psychological impact</td>
<td>13</td>
<td>48%</td>
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<tr>
<td>Too young</td>
<td>8</td>
<td>30%</td>
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<tr>
<td>Limitations of testing</td>
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<td>11%</td>
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<tr>
<td>May influence childbearing</td>
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<td>7%</td>
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<tr>
<td>Legal age</td>
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<td>4%</td>
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n=27 *parents could give more than one reason

Those in favor of genetic testing of minors: Why?

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<thead>
<tr>
<th>Reason</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parents know best</td>
<td>4</td>
<td>31%</td>
</tr>
<tr>
<td>Potential benefits</td>
<td>4</td>
<td>31%</td>
</tr>
<tr>
<td>No reason to withhold</td>
<td>2</td>
<td>15%</td>
</tr>
<tr>
<td>Could influence reproductive decisions</td>
<td>2</td>
<td>15%</td>
</tr>
<tr>
<td>Some children mature enough</td>
<td>2</td>
<td>15%</td>
</tr>
</tbody>
</table>

n= 13 *parents could give more than one reason
Pharmcogenetics & Secondary Information

Pharmacogenomics

“The study of differences between individuals that contribute to the efficacy of drugs or to adverse drug reactions.” *

Goal: “individualizing therapies and improving safety and efficacy of drugs” **

*Netzer, C & Biller-Andorno, N. Bioethics 18:344-360, 2004
**Schubert, L. Bioethics 18:361-378, 2004
The paradigm

Individual with disease X

Test Y

Test Result

Treatment

Emerging Diagnostic Tests

Individual with disease X

Test Y

Test Result

Treatment

ALSO A PREDICTIVE GENETIC TEST
Or susceptibility gene

Germline genetic change that can be passed down through the generations and indicates potential risks for family members
Many of the emerging *genetic diagnostic tests*, including biomarkers and pharmacogenetic tests, also have the potential to be *genetic susceptibility tests* raising unique and unresolved ethical dilemmas.

**Example #1: UGT1A1*28**

Patient with colon cancer to get treatment with irinotecan.

Blood for *UGT1A1*<sup>28</sup> polymorphism

- homozygous

- Reduce irinotecan dose to avoid toxicities
Example #1: *UGT1A1*28

- Blood for *UGT1A1*28 polymorphism
- Patient with colon cancer to get treatment with irinotecan
- homozygous
- Reduced irinotecan dose to avoid toxicities
- * Individuals with a *UGT1A1*28 allele have a 1.8 fold increased risk for breast cancer

What does this mean for family members?

- Females in the family could be tested for the polymorphism
- Consider tamoxifen (chemoprevention)
- May need increased surveillance (MRI, earlier mammograms)
- Avoid hormone replacement therapy or other factors known to increase risks for breast cancer
Example #3: MSI
Microsatellite instability

Patient with stage II colon cancer considering adjuvant chemotherapy

Tumor for microsatellite instability

MSI high

Favorable prognosis

Limited benefit from 5FU-based adjuvant therapy

20% of MSI high patients will have a germline mutation in a MMRG = genetic basis for diagnosis of HNPCC
Cancer Risks in HNPCC

What does this mean for family members?

- IF a mutation is detected…other family members can be tested and consider risk reduction options

  - Screening starting at age 20-25 yo

  - TAH/BSO for female mutation carriers
How do we incorporate such emerging genetic tests?

- How much must be shared with the patient prior to ordering such a test?
- Who should convey the susceptibility information?
  Ordering physician, primary care physician......
- Is genetic counseling required?
- What is our obligation to inform at-risk relatives?
- Who should have access to this information?