The Genetic Component of a Common Disease
The Paradigm of Cancer Genetics
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The Plan
- Introduce/discuss case study
- Epidemiology of cancer
- Tailored prevention
- Resources

The Plan

What’s Going On Here?
- Your neighbor and two of her daughters have had breast cancer. A gentleman across the street died from lung cancer last year, and a young girl next door to him was just diagnosed with leukemia.
- Is there a “true” cluster of cancer on your street? If not chance, what’s the cause?
- How can you as a public health official investigate, understand, and intervene?

Cancer Epidemiology
A Brief Overview
- Lifetime chance ~42% (SEER, 2002)
- Common risk factors
  - Age
  - Diet
  - Smoking (30% of cancer)
- Genetics/Inherited Factors

<table>
<thead>
<tr>
<th>Site</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>All sites</td>
<td>1 in 2</td>
</tr>
<tr>
<td>Prostate</td>
<td>1 in 6</td>
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<tr>
<td>Lung and bronchus</td>
<td>1 in 13</td>
</tr>
<tr>
<td>Colon and rectum</td>
<td>1 in 17</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>1 in 28</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>1 in 46</td>
</tr>
<tr>
<td>Melanoma</td>
<td>1 in 52</td>
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<tr>
<td>Kidney</td>
<td>1 in 64</td>
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<tr>
<td>Leukemia</td>
<td>1 in 67</td>
</tr>
<tr>
<td>Oral Cavity</td>
<td>1 in 73</td>
</tr>
<tr>
<td>Stomach</td>
<td>1 in 92</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Site</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>All sites</td>
<td>1 in 3</td>
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<tr>
<td>Breast</td>
<td>1 in 8</td>
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<tr>
<td>Lung &amp; bronchus</td>
<td>1 in 17</td>
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<tr>
<td>Colon &amp; rectum</td>
<td>1 in 18</td>
</tr>
<tr>
<td>Urinary corpus</td>
<td>1 in 38</td>
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<tr>
<td>Non-Hodgkin lymphoma</td>
<td>1 in 55</td>
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<tr>
<td>Ovary</td>
<td>1 in 68</td>
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<tr>
<td>Melanoma</td>
<td>1 in 77</td>
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<tr>
<td>Pancreas</td>
<td>1 in 79</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>1 in 88</td>
</tr>
<tr>
<td>Uterine cervix</td>
<td>1 in 135</td>
</tr>
</tbody>
</table>

* For those free of cancer at beginning of age interval. Based on cancer cases diagnosed during 2000 to 2002.
† All Sites exclude basal and squamous cell skin cancers and in situ cancers except urinary bladder.
‡ Includes invasive and in situ cancer cases.

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All Cancers: Alcohol (4%), Smoking (29%), Low fruit/vegetable (5%), Indoor smoke from household use of solid fuels (0%), Urban air pollution (1%), Overweight/obesity (3%), Physical inactivity (2%), Contaminated injections in health-care settings (0.5%), Unsafe sex (1%)

Public Health Interventions

- Primary prevention
  - ACS 5-a-day
  - Exercise
  - Prevent smoking initiation
  - Chemoprevention
  - Risk-Reducing Surgery

- Secondary Prevention (Screening)
  - Radiology (Mammography, Colonoscopy, other)
  - Clinical and self-examinations
  - Molecular markers

Lichtenstein et al. NEJM 2000;343(2)73-85
Public Health Interventions

- Tertiary Prevention (Screening)
  - Prevent recurrence and/or new primary
    - Chemotherapy, radiation, surgery, screening
  - Address comorbidity and iatrogenic complications

Challenge of One-Size-Fits-All Approach

- Expensive
- Potentially harmful (unnecessary surgery, radiation exposure, etc.)
- Tailored education may be more effective
- We can do better

How Best To Triage?

- Age
  - Initiating screening appropriately
- Diet
  - Targeted interventions (school lunches, food labeling)
- Genetics
  - Family history
  - Genetic testing

Is It Genetic?

- Cancer clusters
  - Higher-than-expected rate of cancer in geographically-defined area
- Challenges
  - It’s a big country
  - Not coincidence if it happens to you
  - Media influential
  - Are we exploring all the options?

Genetic Cancer Clusters

- 1st-degree relative \( \rightarrow \) RR \( \approx 2-4 \)
- About 25% cancers familial, 5-10% Mendelian
  - Early age
  - Multiple primary cancers
  - Hereditary/Syndromic pattern
  - Positive genetic test

Hereditary Cancer

- Breast Cancer
- Ovarian Cancer

Family tested negative for genetic changes
Long Island Breast Cancer Study

- Overall, modest increase in breast cancer
- Many negative environmental findings
- Family history common risk factor among cases

Family History as a Public Health Tool

- Note Am J Prev Med 2(24); Feb 2003
- Is family history obtained?
- Is it accurate/known?
- Cancer registries
  - VDH (http://www.vdh.state.va.us/epi/cancer/index.asp)
  - MACGN (www.macgn.org)
- Other initiatives
  - http://www.hhs.gov/familyhistory/
  - http://www.cdc.gov/genomics/

Challenges

- Family communication
- Access to expert health services
- Concerns about confidentiality and/or discrimination