“The utility of rapid case ascertainment for a population-based case control study on Hodgkin’s lymphoma”

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Development of our Rapid Case Identification Capability

• Previous work with the Massachusetts Cancer Registry
• Expansion of the Dana Farber/Harvard Cancer Center provided venue for rapid case core
• Our NCI program project (“HL and the Epstein Barr virus”) provided the practicum for getting rapid case to field
Epidemiologic Analysis of the EBV and HL

Study Design: Two companion population-based case-control studies in greater Boston area and the state of Connecticut

Cases: Parallel rapid case identification – about 60 hospitals

Controls: MA - Town Book controls
          CN - Random digit dialing and Medicare lists
Data-gathering

• Telephone interviewing based at Harvard
• Each site handled pathology block retrieval and phlebotomy (cases)
• DNA obtained from population controls by mail (“swish and spit”) via Harvard
Yale Collaborators

• Epidemiology
  Tong Zhang, ScD  co-PI
  Patti Owens

• RCA
  Judith Fine
  Rajni Mehta
The Role of Yale RCA for our Rapid Case Identification Core

- Model
- Mentoring
Utility of Rapid Case Identification to Researchers

• Reduces cost
  – Reduces staff, training, supervision

• Builds on existing relationships with hospitals
  – MD sponsors
  – IRBs
Scientific Utility of using Multiple Sites

• Increases statistical power

• Comparability of data provides verification of internal validity of new findings
  – Example: Aspirin finding
Background

• HL involves the chronic expression of multiple inflammatory mediators
• NF-κB $\uparrow\uparrow$ inflammatory mediators
• In HL, NF-κB $\uparrow\uparrow$ in the cancer cells and appears required for survival and proliferation
• In HL, $\uparrow$ prostaglandins $\uparrow$ inflammatory response and cell division (Cox 1& 2)
Background -2

• Aspirin $\downarrow$ NF-κB by binding to IKK-α in a dose-dependent manner

• Aspirin $\downarrow$ COX 1 & 2 by irreversible binding

• These actions are specific to aspirin among commonly used analgesics
Hypotheses

- Aspirin use is negatively associated with HL

- This association is specific to aspirin among analgesics
Study Population

• Population-based case-control study
  – Greater Boston and State of Connecticut

• Cases: 15-79 at diagnosis (8/1997-12/2000), HIV-negative, alive (N= 507)

• Population Controls: Frequency matched by age group, sex, and state (N= 470)
Data on Analgesics

- Subjects interviewed by telephone
  - average frequency of aspirin, tylenol/acetaminophen, ibuprofen/other NSAID use during the past 5 years

  - composite variable
    - “regular use” = ≥ 2 times weekly
    - “non-users” = < 2 times weekly
# Prevalence of reported medication use

<table>
<thead>
<tr>
<th></th>
<th>Aspirin use</th>
<th></th>
<th>Acetaminophen use</th>
<th></th>
<th>Ibuprofen use</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td><strong>Cases (%)</strong></td>
<td>57 (11%)</td>
<td>450 (89%)</td>
<td>130 (26%)</td>
<td>377 (74%)</td>
<td>109 (21%)</td>
<td>398 (79%)</td>
</tr>
<tr>
<td>**Controls (%)</td>
<td>82 (17%)</td>
<td>388 (83%)</td>
<td>85 (18%)</td>
<td>385 (82%)</td>
<td>105 (22%)</td>
<td>365 (78%)</td>
</tr>
<tr>
<td></td>
<td>139</td>
<td>838</td>
<td>215</td>
<td>762</td>
<td>214</td>
<td>763</td>
</tr>
</tbody>
</table>
ORs* for reported medication use associated with HL

• Aspirin: 0.58 (0.40-0.84)

• Acetaminophen: 1.7 (1.2-2.4)

• Ibuprofen: 0.90 (0.65-1.3)
  – *(adjusted for age, sex, state of residence, and use of other medications)
Internal Validity: Aspirin

• Consistent by age, gender, other medication use

• Consistent by state:

  Massachusetts: $OR_{\text{ADJ}} = 0.54 \ (0.33-0.91)$
  Connecticut: $OR_{\text{ADJ}} = 0.62 \ (0.38-1.00)$
Internal Validity: Acetaminophen

• Consistent by age, gender, other medication use
• Not consistent by state:
  
  Massachusetts: $\text{OR}_{\text{ADJ}} = 2.33 \ (1.54-3.55)$
  Connecticut: $\text{OR}_{\text{ADJ}} = 1.29 \ (0.85-1.96)$
Collaborators

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Mike Borowitz
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Edward Weir

**ViroLab**
Evelyne Lennette

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