EMF Epidemiology: State of the Science

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The Questions

• Driving the issue: leukemia and brain cancer

• New: breast cancer, neurodegenerative and heart disease

• Almost not a question: reproductive outcomes
  – CDHS studies?
Types of Epidemiologic Studies of ELF Exposure

• Residential
  – Wire code
  – Measurements

• Occupational

• Appliance use
Pooled Analyses of Childhood Leukemia

• Greenland et al., *Epidemiology*, 2000
  – 12 studies with fields; 4 with wire codes
  – Not including UK study
  – Field studies: 2,656 cases; 7,084 controls
  – Metric of choice: time-weighted average

• Ahlbom et al., *British J. Cancer*, 2000
  – 9 studies with fields; 2 with wire codes
  – Including UK study
  – Field studies: 3,247 cases; 10,400 controls
  – Metric of choice: geometric mean
Results: Greenland et al., 2000

- 2,145/6,275 cases/controls
- 318/529
- 94/150
- 99/130
Results: Ahlbom et al., 2000

<table>
<thead>
<tr>
<th>Magnetic Field (mG)</th>
<th>Odds Ratio (±95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1</td>
<td>2,866/9,859</td>
</tr>
<tr>
<td>1-2</td>
<td>233/332</td>
</tr>
<tr>
<td>2-4</td>
<td>104/147</td>
</tr>
<tr>
<td>&gt;4</td>
<td>44/62</td>
</tr>
</tbody>
</table>

- ELF
## Measured Fields & Leukemia

<table>
<thead>
<tr>
<th>Summary OR</th>
<th>? 0.1?T (ref.)</th>
<th>&gt;0.1?T, 0.2?T</th>
<th>&gt;0.2?T, 0.3?T</th>
<th>&gt;0.3?T</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Without covariate adjustment</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Woolf</td>
<td>1.00</td>
<td>1.00</td>
<td>0.98</td>
<td>1.91</td>
</tr>
<tr>
<td></td>
<td>(0.82 – 1.21)</td>
<td>(0.68 – 1.40)</td>
<td>(1.37 – 2.67)</td>
<td></td>
</tr>
<tr>
<td>Mantel-Haenszel</td>
<td>1.00</td>
<td>0.98</td>
<td>0.96</td>
<td>1.69</td>
</tr>
<tr>
<td></td>
<td>(0.82 – 1.19)</td>
<td>(0.67 – 1.36)</td>
<td>(1.21 – 2.35)</td>
<td></td>
</tr>
<tr>
<td>Spline</td>
<td>1.00</td>
<td>1.04</td>
<td>1.21</td>
<td>1.83</td>
</tr>
<tr>
<td></td>
<td>(0.93 – 1.17)</td>
<td>(1.02 – 1.43)</td>
<td>(1.14 – 2.93)</td>
<td></td>
</tr>
<tr>
<td><strong>With covariate adjustment</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Woolf</td>
<td>1.00</td>
<td>1.08</td>
<td>0.97</td>
<td>2.14</td>
</tr>
<tr>
<td></td>
<td>(0.87 – 1.35)</td>
<td>(0.65 – 1.44)</td>
<td>(1.49 – 3.08)</td>
<td></td>
</tr>
<tr>
<td>Mantel-Haenszel</td>
<td>1.00</td>
<td>1.03</td>
<td>0.87</td>
<td>2.22</td>
</tr>
<tr>
<td></td>
<td>(0.81 – 1.31)</td>
<td>(0.55 – 1.37)</td>
<td>(1.48 – 3.34)</td>
<td></td>
</tr>
</tbody>
</table>

Greenland et al., 2000
### Pooled Analysis of Childhood Leukemia Studies

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Relative Risks (95% Confidence Intervals)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Measurement</td>
</tr>
<tr>
<td>&lt;0.1 ?T</td>
<td>1.00</td>
</tr>
<tr>
<td>0.1 - 0.2 ?T</td>
<td>1.05 (0.9 - 1.3)</td>
</tr>
<tr>
<td>0.2 - 0.4 ?T</td>
<td>1.15 (0.9 - 1.5)</td>
</tr>
<tr>
<td>&gt;0.4 ?T</td>
<td>1.87 (1.1 - 3.2)</td>
</tr>
</tbody>
</table>

Ahlbom et al., 2000
Conclusions - Pooled Analysis

- A 2-fold increase in risk above 0.3 - 0.4 T
- Association more consistent with measured fields than with wire codes
- Attributable fraction estimate: 3%
- No confounding evident
- Selection bias may be a partial explanation
- Unlikely to be due to random variability
Childhood Leukemia Summary

- Childhood leukemia main driver in risk assessments
- Recent pooling efforts point to risk at 0.3 - 0.4+ T
- Animal studies negative
- Ongoing studies
  - Germany, Italy, Japan, U.S., UK
- Research needs:
  - High-exposure studies
  - Contact currents
  - Population mixing
  - Transients
  - Selection bias
Occupational Leukemia Meta-Analysis
Pooled & Individual Risk Estimates for 38 Leukemia Studies

Kheifets et al.
JOEM, 1997
Occupational Brain Cancer Meta-Analysis

Pooled & Individual Risk Estimates for 29 Brain Cancer Studies

Kheifets et al.  
*JOEM*, 1995
Pooled Risk Estimates for Each Year

Kheifets et al.  
*JOEM*, 1995
Occupational Leukemia & Brain Cancer

• Small risk at the limit of detection
• Few to no studies under way
• Research needs:
  – Exposure assessment based on job and environment
  – Electric fields
  – Combining residential and occupational exposure
  – Contact current exposure assessment
Breast Cancer

• Major women’s health (& public health) issue

• Tied (rightfully or wrongfully) to EMF, based mainly on prior laboratory research

• Hypothesis-based

• Epidemiologic studies largely negative
  – None designed to test the hypothesis
Breast Cancer Summary

• Animal studies inconsistent
  – German results not replicated in the U.S.
• MC-7 cells
  – Effect seen only in certain type of cells
  – Replicated in 3 to 4 laboratories
  – Extremely low exposures
Cardiovascular Disease: Lines of Evidence

Magnetic Field

Human Lab (overnight)

Magnetic Field +/- ? HRV +++ ? CV Risk

Clinical/Epidemiology 1985 – 99

Epidemiology (+/?)

(years – decades)
Cardiovascular Disease

- Association with acute mortality reported in one study
- HRV reduction in laboratory setting apparently inconsistent
- Two analyses of existing data under way
- Research needs:
  - Cardiovascular cause-of-death misclassification on death certificates
Neurodegenerative Diseases

- Increasingly geriatric population
- Suggested risks associated with occupational electrical factors (e.g., jobs, shocks)
- No prior studies specifically designed to examine EMF
- Little ongoing work
- Research needs:
  - Strong methodologic studies looking at electric shocks and other EMF exposures
Reproductive

- Overall negative epidemiologic and laboratory work
- Two recent analyses point to exposures not previously looked at
- Research needs:
  - Evaluate new data
IARC Monographs

- Initiated in 1969
- Criteria established in 1971, last update 1992
- Limited largely to the first step in risk assessment
- “Carcinogen”: exposure that is capable of increasing the incidence of malignant neoplasms (at any stage of the carcinogenesis)
- No recommendation is given with regard to regulation of legislation, as they are the responsibility of governments or other international organizations
- EMF - Volume #80
- 800+ agents have been evaluated
IARC Criteria

• For each disease classify human and animal data separately as:
  • Sufficient
  • Limited
  • Inadequate
  • Lack of effect

• Integrate the two classifications above (*in vitro* as support):
  • Is carcinogenic to humans (Group 1)
  • Probably is carcinogenic to humans (Group 2A)
  • Possibly is carcinogenic to humans (Group 2B)
  • Not classifiable (Group 3)
  • Is probably not carcinogenic to humans (Group 4)
A positive association has been observed between exposure to the agent, mixture or exposure circumstance and cancer for which a causal interpretation is considered by the Working Group to be credible, but chance, bias or confounding could not be ruled out with reasonable confidence.
## Agents Classified by IARC (834)

<table>
<thead>
<tr>
<th>Classification</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carcinogenic to humans (75)</td>
<td>Asbestos, Mustard gas, Tobacco (smoked and smokeless), Gamma radiation</td>
</tr>
<tr>
<td><em>(usually based on strong evidence of carcinogenicity in humans)</em></td>
<td></td>
</tr>
<tr>
<td>Probably carcinogenic to humans (59)</td>
<td>Diesel engine exhaust, Sun lamps, UV radiation, Formaldehyde</td>
</tr>
<tr>
<td><em>(usually based on strong evidence of carcinogenicity in animals)</em></td>
<td></td>
</tr>
<tr>
<td>Possibly carcinogenic to humans (225)</td>
<td>Coffee, Styrene, Gasoline engine exhaust, Welding fumes</td>
</tr>
<tr>
<td><em>(usually based on evidence in humans which is considered credible, but for which other explanations could not be ruled out)</em></td>
<td></td>
</tr>
</tbody>
</table>
The Working Group

Tasks

? Ascertain that all appropriate data have been collected
? Select data based on scientific merit
? Prepare accurate summary to enable reader to follow the reasoning
? Evaluate results of epidemiologic and experimental studies
? Evaluate data relevant to mechanisms of action
? Make overall evaluation of carcinogenicity to humans
The Working Group

Membership

? 23 participants

? Expertise: epidemiology, toxicology, biology, biophysics, statistics, risk assessment, exposure assessment

? 11 countries
Conclusions

- ELF MAGNETIC FIELDS classified as Group 2B “Possible Carcinogenic”
  - based on epidemiologic studies of childhood leukemia
  - animal data inadequate

- Other exposures and outcomes considered “inadequate to classify”
Types of Epidemiologic Studies of RF Exposure

- Populations near antennas and base stations (including cluster studies)
- Occupational/Military personnel studies
- Cell phone users
Critical Exposure Parameters in Cell Phone Studies

- Number of calls and call duration
- Power level of cell phone
- Left- or right-hand use
- User positioning of phone at the face
- Phone type / model
Studies of General Population

- Mostly studies of clusters next to transmitters
- Focus on leukemia; other cancers include brain and bladder cancer and skin melanoma
- Inconsistent results with few statistically significant findings (childhood leukemia?)
Limitations

- Ecologic fallacy
- Small numbers
- Previously identified clusters
- Potential confounding
- Exposure assessment, exposure assessment, exposure assessment
Occupational Studies of RF Exposure

- Few cohort and case-control studies
- Outcomes of interest: leukemia and brain cancer (other outcomes include uveal, testicular, breast and lung cancer)
- Inconsistent, unreplicated results for various cancer types
Limitations

- Job title classification
- Lack of measurements
- Lack of control for potential risk factors
- Use of external comparison groups
Cell Phone Studies

- Three case-control and two cohort studies of cell phone users

- Focus on brain cancer

- Results negative
  - Hints of location of tumor and handedness
Limitations

- Crude assessment
- No measurements
- Low usage (?)
- Short latency
- Hospital controls
• Similar:
  – High public awareness
  • Focus on involuntary exposure from powerlines and antennas
  – Potentially large public health impact
  – Difficulties in exposure assessment exacerbated by unknown biophysical mechanism
Differences

**ELF Studies**
- Much more sophisticated exposure assessment
- More plentiful
- Addressing broader range of outcomes
- Somewhat more consistent

**RF Studies**
- Severely limited by exposure assessment which is likely to be even more difficult than for ELF
- Evolving technology
- Limited by latency
- Only a few outcomes examined (mostly cancer)
- Limited methodologically
Complexities of EMF Science

- Epidemiology
  - Large misclassification
  - Small risk
  - Lack of consistency

- Animal studies
  - Relevant exposure
  - Right model
  - Power to detect small risk

- In Vitro
  - Lack of robust effect
  - Replication
  - Relevance

- Integration
  - Multidisciplinary approach needed
  - Carcinogenesis is a complex and highly variable process