THE ROLE OF EPIDEMIOLOGY IN THE PREVENTION OF ADVERSE HUMAN HEALTH EFFECTS OF NANOTECHNOLOGY

William Halperin, MD MPH DrPH
Jun Tashiro, BA (MD/MPH expected May 2011)

National Nanotechnology Initiative: Human and Environmental Exposure Assessment Workshop
February 24-25, 2009
Charge

• Plenary
  – Characterize health of exposed populations and environments (biota)

• Breakout discussions
  – Identify emerging needs
  – Build a dialogue toward consensus
  – Identify ongoing projects
Outline

1. Cascade of prevention
2. Role of Surveillance
3. Meta-analysis of literature
4. Meta-analysis of research in progress
5. Meta-analysis of grant opportunities
6. Identification of holes
7. Future directions
Basics of Prevention:
The Cascade of Prevention

- Design
- Toxicologic Testing
- Substitution/Elimination
- Engineering Controls
- Environ. Exposure Monitoring
- Personal Exposure Monitoring
- Biological Monitoring
- Medical Screening
- Clinical Care
- Rehabilitation
- Accommodation

References
What is Surveillance and Where is it in the Cascade?

• “Ongoing systemic collection, analysis, and dissemination of exposure and health data on groups of workers for the purpose of early detection of disease and injury as well as patterns of occurrence presumably leading to prevention of subsequent disease.”

Major Types of Studies:
- Registries
- Retrospective
- Prospective

- Accommodation
- Rehabilitation
- Clinical Care
- Medical Screening
- Biological Monitoring
- Personal Exposure Monitoring
- Environ. Exposure Monitoring
- Engineering Controls
- Substitution/Elimination
- Toxicologic Testing
- Design

- Exposure Registries
- Prospective Studies
- Retrospective Studies
Meta-Analyses

1. Published literature?
2. Research activity in pipeline?
3. Research funding opportunities (pre-pipeline)?
Categorization of Literature

- Review articles
- Basic science studies for adverse outcomes / Toxicology
- Basic science studies for beneficial applications
- Clinical trials for beneficial applications
- Clinical trials on adverse health outcomes
- Methods for exposure assessment
- Exposure registries
- Epi: Morbidity studies
- Epi: Mortality studies
- Non-relevant articles
Results of a Systematic Review of Literature

PubMed (1890? – Present)
• nanotechnology & surveillance…39
• nanotechnology & occupational…46
• nanoparticles & surveillance…38
• nanoparticles & occupational…63

Medline (1950 – Present)
• nanotechnology & surveillance…12
• nanotechnology & occupational…32
• nanoparticles & surveillance…8
• nanoparticles & occupational…39

Cochrane Library (1998? – Present)
• nanotechnology…11 (Clinical trials)
  4 (Tech assessments)

154 unique articles
292 total references
References by Year
(n=127)
### References by Category by Year

(n=127)

<table>
<thead>
<tr>
<th>Year</th>
<th>Review</th>
<th>Basic Science: Benefits</th>
<th>Clinical Trials: Benefits</th>
<th>Toxicology</th>
<th>Occupational Exposure Assessment</th>
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RESEARCH IN THE PIPELINE?
Analysis of Grant Awards

• **Source**
  - National Institutes of Health website

• **Limitations**
  - Grant titles; not abstracts
NIH Grant Awards for Research in Nanotechnology, FY 2005 - 2008
An Analysis of NIH FY2008 Grant Awards by Category within a Random Sample

Sample n = 198 (20%)
Total n = 962
Total NIH FY2008 Grant Awards by Category within Random Sample

- **Benefits**
  - Field Development: $3,658,975
  - Basic Science: $199,095,950
  - Toxicology: $7,434,460
  - Engineering: $2,248,610
  - Occupational Exposure Assessment: $1,616,400
  - Exposure Registries: $635,075
- **Hazards**
  - Non-relevant: $22,550,155
  - Unknown: $48,255,305
WAITING TO GO INTO THE PIPELINE?
Analysis of Federal Grant Opportunities

• **Sources**
  – Grants.gov (includes military, non-NIH / NSF)
  – National Institutes of Health
  – National Science Foundation

• **Method**
  – Automated search for “nanotechnology” or “nanoparticle(s)”; manual filtering for health issues
  – Review of RFA titles and abstracts
Grant Funding Opportunities for Research on Adverse Health Outcomes

**Grants.gov (Federal)**
- nanotechnology... 42
- nanoparticle(s) ... 7

**National Institutes of Health**
- nanotechnology... 21
- nanoparticles... 5

**National Science Foundation**
- nanotechnology... 23
- nanoparticles... 6

As of Feb 1, 2008
Grant Funding Opportunities for Research by Category (n=56)
Holes

- Non-published research
- Non-governmental research funding
- Non-funded registries
- Best practices survey for bio-monitoring; medical monitoring
- Development of epidemiologic methods

- Biomonitoring
- Medical monitoring
- Morbidity
- Mortality
- Workers, residents, and biota
WHAT NEEDS TO BE DONE?
Methods development
After Identifying Potentially Exposed

- Biomonitoring
  - For nanoparticles, in human samples
- Medical monitoring and testing
- Epidemiologic methods
More on Limitations: Will Prototypical Surveillance Systems Work?

<table>
<thead>
<tr>
<th></th>
<th>NIOSH Preplanned Cohort Studies</th>
<th>CPSC Sentinel Hospitals (e.g. NEISS)</th>
<th>FDA Passive Post-market Surveillance</th>
<th>NIOSH Field Epidemiology and Investigation</th>
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<td>Local Human - Occupational</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+</td>
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<tr>
<td>Widespread Human - Environmental</td>
<td>+</td>
<td>+</td>
<td>+/-</td>
<td>+</td>
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<tr>
<td>Local Plant life</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+</td>
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<tr>
<td>Local Non-human animal life</td>
<td>+</td>
<td>-</td>
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A Strategic Approach to Population-based Research

- All nanotechnology
- Consensus on potential hazards
- Exposure assessment
- Morbidity studies and registries
- Mortality studies and registries

Reactive
Organizing and Managing the Process

- Academics
- Regulators
- Clinical and Public Health
- Industry
- Labor
- Progress
TOGETHER WE WIN
Get behind your labor-management committee
Humility:

“Good surveillance does not necessarily ensure the making of the right decisions but it reduces the chances of wrong ones.”

- Alex Langmuir
Summary and Conclusions:

• A wave of beneficial new technology is coming
• There may be exposures and related hazards
• We need:
  – To be organized and inclusive
  – To be systematic and judicious
  – To be funded (set aside of 5-10% of funding)
THE END


Literature: Basic Science Benefits


Literature: Clinical Trials Benefits


Literature: Nanotoxicology


Literature: Occupational Exposure Assessment


Grants: Field Development

- Career Development Component ($66,268)
- Training for a New Interdisciplinary Research Workforce in Regenerative Medicine ($331,407)
- Nanobiology Institutional Training Grant (RMI) ($318,605)
- Priority Setting Stage ($15,042)
Grants: Basic Science Benefits

- Use of Beta-lapachone for Lung Cancer Chemotherapy ($341,159)

- Using Nanomaterials to Inhibit Mast Cell/Basophil-Associated Disease ($297,814)

- Viral Detection Using Fluorescent Nanocrystals ($330,353)

- Tumor targeted RNAi by novel nanovectors for molecular therapy of prostate cancer ($127,680)
Grants: Occupational Exp Assessment

- Nontoxic Si Nanoprobes for Multiple Biomarker Imaging ($323,280)
Grants: Engineering

- Atomic force microscope ($275,000)

Grants: Exposure Registries

• Development of methods and models for nanoparticle toxicity screening ($127,015)
Grants: Toxicology

- Chemical, Structural, and Superstructural Determinants of Nanocarbon Toxicity ($249,900)

- Nano-Biological Interactions and Toxicity of Engineered Metal Oxide Particles ($346,500)

- Pharmacology and Toxicology Core ($413,290)

- Remote Microvascular Dysfunction After Particulate Matter Exposure ($477,202)
Funding Opportunities: Field Development

• Ethics Education in Science and Engineering (NSF)

• Science, Technology, and Society (NSF)
Funding Opportunities: Basic Science

Benefits

• FY 2009 Multidisciplinary University Research Initiative (MURI) - For Proposal Submission to the Air Force (Air Force Office of Scientific Research)

• Metallic Materials and Nanostructures (NSF)

• Nanoscience and Nanotechnology in Biology and Medicine (R01) (NIDCR)

• Nanotechnology Undergraduate Education in Engineering (NSF)
Funding Opportunities: Exposure Assessment

- Environmental Implications of Emerging Technologies (NSF)
- Research to Action: Assessing and Addressing Community Exposures to Environmental Contaminants (R21) (NIEHS)
- Superfund Basic Research and Training Program (P42) (NIEHS)
Cascade of Prevention


