



Chemical Agents of Opportunity for Terrorism: TICs & TIMs

After-Event Medical Monitoring: Pros and Cons

Chemical Agents of Opportunity for Terrorism:
TICs & TIMs

Medical Monitoring

- What is medical monitoring?
- Should it be done?
- If so, when and how?
- Can it be done in a mass casualty situation?

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Medical Monitoring

Ongoing or serial evaluation (clinical and/or laboratory) of individuals in order to identify adverse effects following their exposure to some substance.

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Medical Monitoring

- Divisive, emotional concept or term
- Often claimed and maligned in the toxic tort system
 - Federal Employer’s Liability Act of 1909
 - Metro North Commuter Railroad vs. Buckley (1997)
 - Silicone breast implants, Phen-Fen, Vioxx?



Example: Clinical Monitoring

- Methylisocyanate-induced reactive airways disease
 - Peak flow measurements
 - ?Methacholine challenge testing
 - ? removal of those with previous/underlying asthma or atopic conditions



Example: Laboratory Monitoring

- Using cholinesterase measurements as rule-out tests for nerve agent or organophosphate exposure
 - Population norms for plasma cholinesterase
 - Confirmatory testing by RBC Cholinesterase or serial plasma cholinesterase

Medical Monitoring in Biopreparedness

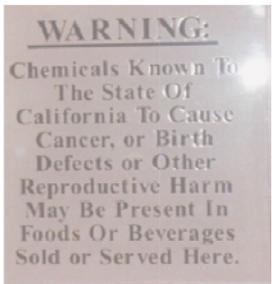
POTENTIAL AGENTS	MONITORING CAPABILITY?	
	Clinical	Laboratory
Cyanide.....		
Incapacitating Agents.....	Rapid knock-down	Slow
Volatile Organic Compounds.....	Irritants/Sedatives	No
Industrial Contaminants.....	CNS depressants	No
Industrial Solvents.....	Variable organ effects	No
Heavy Metals.....	CNS/other organs	No
Nerve Agents.....	CNS/other organs	Slow
Mustard Agents.....	Cholinergic crisis	Yes
	Skin/Pulmonary	No

Medical Monitoring

- Presumes an injury may or will occur
- Presumes an exam or test will identify:
 - Those at risk
 - The injury itself, hopefully at an early stage
- Best utilized when an effective treatment or mitigation can be done

The Existence of a Test Does Not Mean We Know What To Do With The Results

- CA Prop 65
 - The Safe Drinking Water and Toxic Enforcement Act of 1986
- Currently over 700 substances on list
- No dose/response consideration
- http://www.oehha.org/prop65/prop65_list/files/070904list.html





The Future of Biomonitoring: National Academy of Science Report 2006

- The relative value of biomonitoring efforts is dependant on what is communicated
- Is the sample population representative?
- Are the methods and analysis sound?
- Descriptive vs. Risk-based communication?

The National Academy of Sciences Report on
Biomonitoring, July 2006:
<http://newton.nap.edu/catalog/11700.html>

Interpretation and Communication of Biomonitoring Information

- Many groups have begun biomonitoring initiatives
 - CDC/NCEH National Report on Human Exposure to Environmental Chemicals
<http://www.cdc.gov/exposurereport/>
 - Stringent laboratory science with descriptive and some risk-based interpretation
 - California Environmental Contaminant Biomonitoring Program
<http://www.calepa.ca.gov/Legislation/2006/SB1379.pdf>
 - Revised to incorporate risk communication
 - Environmental Working Group
<http://www.ewg.org/bodyburden/>
 - "Nice" website with no information for comparison/interpretation

Interpretation and Communication

- Descriptive vs. Risk-Based Interpretation
 - Descriptive
 - Presence and concentration of a compound in the 50th, 95th percentiles of population
 - How well does the sample population mimic the population of interest?
 - How well do the exposure settings match?
 - » Acute vs. chronic
 - Are the matrices (e.g. blood, urine) the same or are there conversion estimates available?

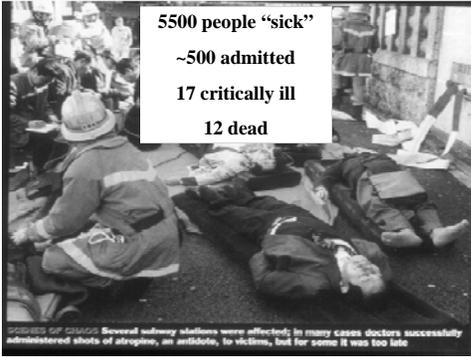
Interpretation and Communication

- Risk-based interpretation
 - Good data only available for some compounds
 - Usually requires modeling and extrapolation
 - Does the primary literature (animal, human epidemiologic) adequately address dose range and potential confounders?
 - For any postulated low-level exposures, difficult to sort out confounders from genetically “sensitive population”
 - Mostly speculation

Applying Medical Monitoring To A Terrorist or HazMat Event

- Sarin Tokyo Event
 - Cholinesterase monitoring of patients
 - Serial exams of exposed healthcare providers
- Radiation workers
 - External/Internal Contamination vs. “radiated”
- Seveso, Italy
 - Acute and chronic effects
- South Wales, 1995
 - Perception

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Nerve Agent vs. Anxiety/Stress Response

Nerve Agent Poisoning	Anxiety/Stress Response
Chest Tightness	Chest Tightness
Dyspnea	Dyspnea
Brady or Tachycardia	Tachycardia
Nausea/Vomiting	Nausea/Vomiting
Abdominal Cramps	Abdominal Cramps
Involuntary Urination	Involuntary Urination
Fasciculations	Tremor
Headache	Headache
Coma	Syncope
Diaphoresis	Diaphoresis
Pinpoint Pupils	Dilated Pupils

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Radiation Medical Monitoring

- Goiania, Brazil: Sept 1987
 - Dismantling of an abandoned Cs-137 radiotherapy source results in dispersal and distribution of radioactive cesium
 - Over 100,000 people surveyed for contamination
 - 249 identified; 4 deaths
 - "Radioactive" biomonitoring tool would be the Geiger counter



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...And now: Polonium-210

- **UNITED KINGDOM: 100 test positive for polonium exposure**

More than 100 people have tested positive for polonium-210 exposure during investigations into the death of the former Russian agent Alexander Litvinenko, the Health Protection Agency (HPA) revealed yesterday. Thirteen have been told they received a dose above six millisieverts, which increases the lifetime risk of cancer by 0.005%. The HPA has tested almost 600 people in the vicinity of the hotels and restaurants where radioactive traces were found. Of these, 73 received doses of less than one millisievert and 30 received up to six millisieverts - levels the HPA said posed no public health risk. Alok Jha

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Seveso, Italy 1976

- Worst environmental exposure to TCDD
- Early rise in induced abortions and circulatory deaths
- Late statistically significant rise in non-Hodgkin's lymphoma (Relative Risk 2.8, with CI: 1.1, 7)
- Significance of lymphoma risk?
 - Baseline incidence 10/100,000 or so
- Risk communication?
 - U.S. <10 ppt (vs >200 ppt in Seveso-exposed)



Zone	Population 20-75 ans	Contamination du sol en µg/m3 (min – max)
A	735	15.5 - 580
B	4700	1.7 - <50
R	31800	0.9 - <5

<http://www.mines.inpl-nancy.fr/~verdel/cindv/fiches2001/seveso.php>

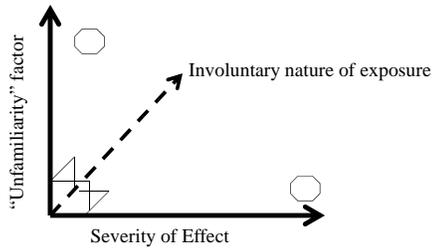


Sea Empress Oil Spill 1996

- 70,000 tonnes of oil spilled into an environmentally sensitive area
- 39% of residents near the spill complained of persistent headaches, irritative, or psychological symptoms
- 20% of people in unaffected, but nearby areas, complained of similar symptoms, with perhaps 1 of 5 thinking their symptoms were related to the oil spill



Degree of Outrage



Should Medical Monitoring Be Considered?

- Only in larger context of risk communication
- Clinical Monitoring: Only if a clinical measurement is demonstrated to have good correlation
 - Problem of screening and specificity/sensitivity
- Laboratory Monitoring: Only if a reference measurement is available
 - E.g. population measurements by NHANES

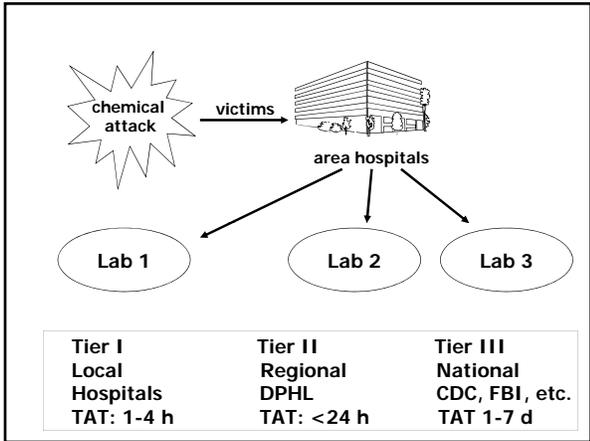
Testing Paradigm

- Therapeutic monitoring
 - High pre-test likelihood, looking for high precision
- Diagnostic Testing
 - Rule-in
 - Moderate pre-test likelihood, high sensitivity (few false negatives)
 - Rule-out
 - Low-moderate pre-test likelihood, high specificity (few false positives)
- Screening
 - Low pre-test likelihood, looking for high sensitivity



The Influence of Prevalence on Drug Testing Assays

10,000 subjects	Nonusers	Users	Prevalence: 1% Test accuracy: 99%
	9,900	100	
True negative	9801	99	True positive
	99	1	





Example: Response to Community Concern

- “Everyone is being poisoned by <fill in the blank>”
- Let’s use mercury as an example
 - Good population data
 - Good clinical harm data for overt effects
 - Data for “low-level” or “special population” effects?

Common Example

- School custodian is cleaning a science room
- Notes silver globules over floor and in hallway
- Notices...
- School evacuated – 300 children
- Shoes evaluated for mercury contamination
- Children sent home, some wrapped in blankets
- Parents ask...
 - what happened?
 - what should I do?
 - are my children safe?



School Mercury Exposure

- Risk Assessment
 - Environmental mercury contamination
 - Duration and extent must be defined
 - Environmental measurements
 - Air and shoes/clothing
- Risk Communication
 - “There is no health risk from this event”
 - “There is no need for medical monitoring in this situation”
 - “We are taking extra precautions to prevent tracking of the mercury elsewhere”



Each Situation Needs To Be Evaluated...

- Host – Susceptible children
- Duration – hours/daily
- Dose - ???

NEW JERSEY INQUIRY PLANNED INTO DAY-CARE MERCURY LEVELS
FRANKLINVILLE, N.J. — New Jersey’s attorney general has ordered an investigation into why a day-care center where dozens of children were exposed to toxic mercury fumes was allowed to operate in a former thermometer factory. Attorney General Zulima Farber called the situation at Kiddle Kollege “outrageous.” The center closed July 28 after owners were told of the mercury fumes, and officials said more than 30 children were exposed to toxic mercury vapors at the center.

Legislation and Lawsuits: Best Answer?

- **Governor signs law for air-quality checks at day care centers**
Angela Delli Santi / Associated Press Writer Thu January 11, 2007 13:36 EST

FRANKLIN TOWNSHIP, N.J. (AP) _ The air quality of new day-care centers in New Jersey will have to be monitored under a measure signed into law by Gov. Jon S. Corzine on Thursday in a Gloucester County town where children attending one facility were contaminated by high levels of mercury...

The bill was signed in Franklin Township, the same small southern New Jersey community where more than 30 children were exposed to toxic mercury vapors while attending Kiddie Kollege, a day care on the site of a former thermometer factory. A second center, also closed, was atop a former fuel company. A third sits at a former gas station that has leaking underground tanks.

The state Department of Environmental Protection found mercury levels at Kiddie Kollege were **25 times the allowable limit** during a random....

Summary

- Post-event medical monitoring may be indicated
- Medical monitoring is only one component of risk assessment and communication
- If performed, medical monitoring requires defined clinical and/or laboratory parameters and must be done with an appropriate control group
- Healthy skepticism is important in interpretation of medical monitoring data
