Chemical Agents of Opportunity for Terrorism: TICs & TIMs

Module Eleven:
Post-Event Medical Monitoring: Pros and Cons

Charles McKay, MD, FACMT
American College of Medical Toxicology
Doug Meckes, DVM
State Veterinarian, North Carolina
March 9, 2016
Course Overview

1. Introduction / Principles of Medical Toxicology
2. Why Toxic Industrial Chemicals as Terrorist Weapons?
3. Inhalation of Toxic Industrial Gases
4. Agricultural Chemicals of Concern
5. Cyanide and Fumigants
6. Psychological Consequences of Mass Chemical Exposure
7. Risk Communication
8. Neurotoxins
9. Water, Food, and Medication as Vectors
10. Delayed-Onset Toxins
11. Post-Event Medical Monitoring
12. Roundtable Discussion / Wrap-up
Please help us improve this course by filling out the course evaluation.

You will receive an email with instructions following the conclusion of this course.
Faculty Disclosure

• Faculty: Charles McKay, MD, FACMT
• Relationships with commercial interests: none
  – Speakers Bureau/Honoraria: none
  – Consulting Fees: none
  – Other: none
Faculty Disclosure

• Faculty: R. Douglas Meckes, DVM
• Relationships with commercial interests: none
  – Speakers Bureau/Honoraria: none
  – Consulting Fees: none
  – Other: none
Participant Question:

- How many people are in attendance at your site (including yourself)?
Medical Monitoring: Objectives

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

Ongoing or serial evaluation (clinical and/or laboratory) of individuals in order to identify adverse effects following their exposure to some substance.
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, asymptomatic smokers, …?
Example: Clinical Monitoring

• Methylisocyanate-induced reactive airways disease
  – Peak flow measurements
  – Methacholine challenge testing
  – Removal of those with previous/underlying asthma or atop 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

- Cyanide
- Incapacitating Agents
- Volatile Organic Compounds
- Industrial Contaminants
- Industrial Solvents
- Heavy Metals
- Nerve Agents
- Mustard Agents

### MONITORING CAPABILITY?

<table>
<thead>
<tr>
<th>Clinical</th>
<th>Laboratory</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid knock-down</td>
<td>Slow</td>
</tr>
<tr>
<td>Irritants/Sedatives</td>
<td>No</td>
</tr>
<tr>
<td>CNS depressants</td>
<td>No</td>
</tr>
<tr>
<td>Variable organ effects</td>
<td>No</td>
</tr>
<tr>
<td>CNS/other organs</td>
<td>No</td>
</tr>
<tr>
<td>CNS/other organs</td>
<td>Slow</td>
</tr>
<tr>
<td>Cholinergic crisis</td>
<td>Yes</td>
</tr>
<tr>
<td>Skin/Pulmonary</td>
<td>No</td>
</tr>
</tbody>
</table>
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 800 substances on list
- No dose/response consideration
- [http://oehha.ca.gov/prop65/prop65_list/files/P65single061915.pdf](http://oehha.ca.gov/prop65/prop65_list/files/P65single061915.pdf)
Chemical Agents of Opportunity for Terrorism: TICs & TIMs
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?

Interpretation and Communication of Biomonitoring Information

- Many groups have biomonitoring initiatives
    - Stringent laboratory science with descriptive and some risk-based interpretation
    - Revised to incorporate risk communication
    - “Nice” website; no information for comparison or 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. “irradiated”
• Seveso, Italy
  – Acute and chronic effects
• South Wales, 1995
  – Perception
Chemical Agents of Opportunity for Terrorism: TICs & TIMs

5500 people “sick”
~500 admitted
17 critically ill
12 dead
## Chemical Agents of Opportunity for Terrorism: TICs & TIMs

### Module 11 – Post-Event Medical Monitoring: Pros and Cons

#### Nerve Agent vs. Anxiety/Stress Response

<table>
<thead>
<tr>
<th>Nerve Agent Poisoning</th>
<th>Anxiety/Stress Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest Tightness</td>
<td>Chest Tightness</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>Dyspnea</td>
</tr>
<tr>
<td>Brady or Tachycardia</td>
<td>Tachycardia</td>
</tr>
<tr>
<td>Nausea/Vomiting</td>
<td>Nausea/Vomiting</td>
</tr>
<tr>
<td>Abdominal Cramps</td>
<td>Abdominal Cramps</td>
</tr>
<tr>
<td>Involuntary Urination</td>
<td>Involuntary Urination</td>
</tr>
<tr>
<td>Fasciculations</td>
<td>Fasciculations</td>
</tr>
<tr>
<td>Headache</td>
<td>Headache</td>
</tr>
<tr>
<td>Coma</td>
<td>Coma</td>
</tr>
<tr>
<td>Diaphoresis</td>
<td>Diaphoresis</td>
</tr>
<tr>
<td>Pinpoint Pupils</td>
<td>Pinpoint Pupils</td>
</tr>
<tr>
<td></td>
<td>Pinpoint Pupils</td>
</tr>
</tbody>
</table>

|                       |                       |
|                       | Dilated Pupils        |

- **Nerve Agent Poisoning** includes symptoms such as chest tightness, dyspnea, brady or tachycardia, nausea/vomiting, abdominal cramps, involuntary urination, fasciculations, headache, coma, diaphoresis, and pinpoint pupils.

- **Anxiety/Stress Response** includes symptoms such as chest tightness, dyspnea, tachycardia, nausea/vomiting, abdominal cramps, involuntary urination, tremor, headache, syncope, diaphoresis, and dilated pupils.
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Module 11 – Post-Event Medical Monitoring: Pros and Cons

Chemical attack

victims

area hospitals

Lab 1
Lab 2
Lab 3

Tier I
Local
Hospitals
TAT: 1-4 h

Tier II
Regional
DPHL
TAT: <24 h

Tier III
National
CDC, FBI, etc.
TAT 1-7 d
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
...And more recently: 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.

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Radiation Medical Monitoring

• Exposure to source of ionizing radiation
  – Iridium 192 gamma radiation emitter
    • 0.5 x 0.5 mm core with 1 Ci of activity
• Irradiated NOT radioactive
• Absolute lymphocyte count as a prognostic tool
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)

<table>
<thead>
<tr>
<th>Zone</th>
<th>Population 20-75 ans</th>
<th>Contamination du sol en µg/m³ (min - max)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>735</td>
<td>15.5 - 580</td>
</tr>
<tr>
<td>B</td>
<td>4700</td>
<td>1.7 - &lt;50</td>
</tr>
<tr>
<td>R</td>
<td>31800</td>
<td>0.9 - &lt;5</td>
</tr>
</tbody>
</table>

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, irritive, or psychological symptoms
- 20% of people in unaffected, but nearby areas, complained of similar symptoms, with 1 in 5 thinking symptoms were related to the oil spill
Degree of Outrage

“Unfamiliarity” factor

Severity of Effect

Involuntary nature of exposure
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
Example: Response to Community Concern

• “Everyone is being poisoned by &lt;fill in the blank&gt;”

• 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
• Notifies...
• 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?
Participant Question:

What plan do you want to implement?

a. Obtain blood and urine Hg on all
b. Obtain blood and urine Hg on some
c. Obtain urine protein determinations
d. Begin immediate chelation of all
e. Begin immediate chelation of some
f. Work with the school and FD to develop response/cleanup system
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”
However, each Situation Needs To Be Evaluated…

- Day care center housed in previous thermometer factory
  - Exposed group: 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 Kiddie 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.
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 check of the site in July, prompting the building to be shut. Subsequent tests showed the preschool students had elevated levels of mercury, but officials said the effects of the exposure should not be long-term.

The state filed a lawsuit against the current and former owners of the site last month, claiming that environmental officials have been denied access to the site since Kiddie Kollege closed in August. The families of several children enrolled at Kiddie Kollege have filed their own lawsuits...

The state Attorney General's office is looking into how the center, which opened in 2004, was allowed to operate without a cleanup of the mercury.

Wolf Skacel, assistant DEP commissioner for compliance and enforcement, said the agency has thus far inspected 142 of the 1,400 day cares located within 400 feet of a site that DEP regulates. Those include dry cleaners and other businesses for which the environmental agency issues permits, as well as contaminated sites, Skacel said.

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Melamine

- Chemical reagent for dyes, cosmetics, plastics, fire retardants, construction material
- High nitrogen content
- “Low toxicity” rating: mouse LD50 of ~3g/kg
- First in the news in 2007 with pet food contamination as part of the widespread “Made in China…” scandal
- Intentional adulterant to falsely boost apparent protein content

http://www.who.int/foodsafety/fs_management/Melamine.pdf
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- Nitrogen source needed for plant growth and as protein “building block” for ruminants
- Ammonia is OK for plants; may be harmful in large amounts for animals
- Urea and its condensation product (biuret) are OK in small amounts (bacterial conversion)
- Melamine was considered, but “releases” nitrogen too slowly to be preferred
2007 Melamine Tainted Pet Food
2007 Melamine Tainted Pet Food

Timeline

Nov. 2006
• Tainted Wheat Gluten shipped from China to United States
• Tainted Wheat Gluten used in Pet Food Production by Menu Foods

Feb 2007
• Menu Foods receives reports of sick pets

March 2007
• Menu Foods begin wet pet food recalls, about of 1% of all pet food in marketplace
• Melamine found in urine and kidneys of sick cats and pet food
• Menu Foods confirms wheat gluten is the cause, expands recall of wet pet food produced in the US
• FDA confirms the presence of melamine in imported wheat gluten from China
• More than 150 pet food brands voluntarily recalled
2007 Melamine Tainted Pet Food Timeline

April 2007

- Banfield Pet Hospital reports a 30% increase in kidney failure at its 615 veterinary hospitals in the US for 1st quarter of 2007. 3 out of 10,000 cats/dogs developed kidney failure
- Veterinary Information Network web site reports 471 kidney failures reported and 100 deaths from its 30,000 member US veterinarians
- FDA admits in Senate hearing contaminated food still on store shelves
- Wilbur-Ellis Company finds melamine bag in shipment of rice protein concentrate from China, contacts FDA
- Melamine confirmed in Wilbur-Ellis rice protein concentrate, concentrate was sent to 5 pet food manufacturers
- Discovery that rice protein concentrate from Wilbur-Ellis supplier also used in hog feed.
- FDA reports melamine discovered in hog urine
2007 Melamine Tainted Pet Food

Timeline

April 2007

- FDA reports cyanuric acid found in imported glutens
- 6000 hogs quarantined in California
- FDA & USDA announce contaminated feed was fed to broiler chickens at 38 farms and millions may have been consumed
- FDA orders that all vegetable protein imports from China used in human and animal food be detained.
- FDA report 330 of 750 samples of wheat gluten and products with wheat gluten tested positive for melamine contamination. 27 samples of 85 rice protein concentrate and products made with it were contaminated.
- FDA Officials traced the melamine responsible for pet deaths to two Chinese plants, which have been supplying American distributors since 2006.
2007 Melamine Tainted Pet Food

Results

May 2007

- Chinese authorities detain Mao Lijun, general manager of the Xuzhou Anying Biologic Technology Development, supplier of tainted wheat gluten
- Zheng Xiaoyu, the head of the Chinese State Food and Drug Administration from its founding in 1998 until 2005 receives the death sentence for corruption
- China also announces the creation of its first recall system for unsafe food products

Owners and executives of Xuzhou Anying Biologic Technology Development Company, Suzhou Textiles, Silk, Light Industrial Products, Arts and Crafts, and ChemNutra were indicted on charges of intentionally defrauding and misleading American manufacturers about poisonous ingredients used in pet food
2007 Melamine Tainted Pet Food

Results

The biggest pet food recall in history, involving about 180 brands and some of the most prominent names in the business — Hill’s Pet Nutrition, Mars Inc., Del Monte Pet Products, Nestle Purina PetCare Co., The Iams Co. and Procter & Gamble among them — as well as dozens of retailers, including Wal-Mart, Target, PetSmart, Petco and Costco. The majority of products came from Menu Foods, a Canadian company contracted to manufacture numerous brand-name and private label pet foods.

Pet owners whose pets had eaten food contaminated with melamine filed a suit against Menu Foods that settled for $24 million.

Economic Adulteration - testing and investigation in Canada, the US, and China revealed the deliberate introduction, by a Chinese-sourced manufacturer, the unauthorized additive melamine into wheat gluten, to artificially boost measured protein levels in order to improve the quality rating of sub-standard product.
2007 Melamine Tainted Pet Food Response

Food and Drug Administration Amendments Act of 2007 (FDAAA)
- The law mandates that the HHS Secretary “establish an early warning and surveillance system to identify adulteration of the pet food supply and outbreaks of illness associated with pet food
- FDAAA directs the Secretary of Health and Human Services, in consultation with the Association of American Feed Control Officials (AAFCO) and other relevant stakeholder groups, to establish ingredient standards and definitions, processing standards, and updated labeling standards for pet food within two years of the date of enactment of the legislation.

Food Safety Modernization Act (FSMA) 2011
- CVM Animal Feed Safety System (AFSS) was to describe how animal feeds should be manufactured and distributed to minimize risks to animals that consume animal feeds and humans that consume food products from animals
2007 Melamine Tainted Pet Food Response

Food and Drug Administration Amendments Act of 2007 (FDAAA)
FDA response May 2008 meeting
“Requirements, if limited to pet food only, would be impractical to implement, difficult to enforce, and would not effectively provide the safety enhancements intended by FDAAA. The standards mandated by FDAAA do not currently exist for any animal food or feed, limiting new requirements to pet food only would fail to address the broader food safety concerns associated with food intended for other animal species, particularly food-producing animals”

GC-MS Screen for the Presence of Melamine, Ammeline, Ammelide, and Cyanuric Acid Laboratory Information Bulletin 4423 Vol 24 October 2008
Foreign Supplier Verification Programs for Food Importers (FSVP). importers are now responsible for assuring that the food they import complies with FDA requirements. They must determine hazards and evaluate risk parallel the preventive control rules for human food (PCHF) and animal food (PCAF).
Melamine Cases: Animals as Sentinels

- 2007: Cases of renal failure in cats and dogs
- 2007: (Very) rare human effects from eating pet food
- 2007: Unfounded concern about trace contamination of animal food products
- 2008: Initial reports of infants in China ill, developing renal failure, and some deaths
Human Toll

• ~4 children dead (none in US)
• 12,000 => 20,000 hospitalized (none in US)
• 52,000 => 100,000 sickened (none in US)
• Recrimination and resignations (none in US)
• Rumors (many in US)
  – Kraft’s response: “no milk products” in Oreos
  – “no safe amount”: FDA Oct. 3 2008
Chinese milk scandal engulfs White Rabbit candy

Production of the beloved sweets has been halted because of suspected melamine contamination.

From the Associated Press
September 29, 2008

BEIJING — They were Premier Zhou Enlai's favorite late-night snack. He loved White Rabbit candy so much he gave a bag to U.S. President Richard Nixon during his historic visit to China. But the brand, beloved by generations of Chinese, took a hit after it was linked to the tainted milk scandal.

The Shanghai-based maker of the candy said Friday that it had halted production because of suspected melamine contamination. The chewy vanilla-flavored White Rabbit sweets have been pulled from store shelves around Asia and in Britain after the candy was linked to the tainted milk scandal.

The Ge Yi Sheng Yuan Co. was still waiting for test results on samples of its exported products, but all sales had been stopped as a precaution, said Ge Junjie, a vice president of Eight Foods Co., which owns the Shanghai maker.

"It's a tragedy for the Chinese food industry and a big lesson for us as it ruined the time-honored brand," he was quoted as saying by the Shanghai Daily.

The Associated Press

Cadbury recalls Chinese-made chocolates

Firm says tests 'cast doubt' on product safety amid fallout over tainted milk

Cadbury chocolates in a store in Beijing on Monday.

HONG KONG — British chocolate maker Cadbury said Monday tests have "cast doubt" on the safety of its Chinese-made products and ordered a recall, the latest foreign company affected by China's tainted milk scandal.

Tests "cast doubt on the integrity of a range of our products manufactured in China," Cadbury said without elaboration in a statement issued from its office in Singapore.

It wasn't immediately clear whether the tests revealed melamine, the industrial chemical at the center of China's recent milk scandal.

Story continues below →
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Module 11 – Post-Event Medical Monitoring: Pros and Cons

Degree of Outrage

“Unfamiliarity” factor

Involuntary nature of exposure

Severity of Effect
Request for biomonitoring after a community-wide exposure

( Participant Question )

What kind of test would be best if the substance carries a risk of delayed onset of chronic lung disease?

a. Yearly chest x-rays
b. Mailed symptom questionnaire
c. Limited spirometry (peak flow measurements)
d. Both b. and c.
e. Bronchoscopic lung biopsy or lavage fluid assessment
f. Both b. and e.
Request for biomonitoring after a community-wide exposure

(Participant Question)

What kind of test would be best if the exposure seems limited in scope and extent, but an occupational BEI (Biological Exposure Index) is available?

a. First morning voided urine analysis of the substance in comparison to its BEI
b. Screening as in a., but only of workers (since the BEI is occupationally-derived)
c. No biological testing is indicated
d. Measurement as in a., but with all results normalized by urine creatinine measurement
Request for biomonitoring after a community-wide exposure

What kind of test would be best if the exposure seems limited in scope and extent, but an occupational BEI (Biological Exposure Indices) is available?

1. First morning voided urine measurement of the substance in comparison to its BEI
2. Screening as in 1., but only of workers (since the BEI is occupationally-derived)
3. No biological testing is indicated
4. Screening as in 1., but with all results normalized to urine creatinine measurement
Summary

• Post-event medical monitoring may be indicated in the assessment of an exposure
• 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 interpreting reported medical monitoring data
Questions?
Appendix

• Sorting out screening from ‘rule-in’ and ‘rule-out’ testing

• Importance of recognizing role of disease prevalence when evaluating ‘positive’ tests (even with high sensitivity and specificity)
Testing Paradigm

• Therapeutic monitoring
  – High pre-test likelihood, looking for high precision

• Screening
  – Low pre-test likelihood, looking for high sensitivity

• Diagnostic Testing
  – Rule-out [SnNout]
    • Low to moderate pre-test likelihood, high sensitivity test negative
      (few false negatives)
  – Rule-in [SpPin]
    • Moderate pre-test likelihood, high specificity test positive
      (few false positives)
Interplay of Sn and Sp

- Even very specific tests will have low positive predictive value if sensitivity is low.
- Even very sensitive tests will have low negative predictive value if specificity is low.
The Influence of Prevalence on Drug Testing Assays

10,000 subjects

<table>
<thead>
<tr>
<th>Nonusers</th>
<th>Users</th>
</tr>
</thead>
<tbody>
<tr>
<td>True negative</td>
<td>9801</td>
</tr>
<tr>
<td>False positive</td>
<td>99</td>
</tr>
</tbody>
</table>

Prevalence: 1%
Test accuracy: 99%

- True positive: 99
- False negative: 100
- True negative: 9801
- False positive: 99

10,000 subjects * 0.1% = 10
10 * 0.99 = 9.9

10 - 9.9 = 0.1

9,900
100