“Med-X”:
Medical Examiner Surveillance for
Infectious Disease & Bioterrorism Mortality

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Infectious Disease Emergence

- Increased incidence within past 20 years
- Threatened increase in near future
- Bioterrorism - subset of emerging infections
May 14, 1993

NM Unexplained Deaths, 1993

<table>
<thead>
<tr>
<th>OMI reports 3 deaths</th>
<th>IHS reports 5 deaths</th>
<th>CDC, ID, toxicology experts consulted</th>
<th>Families interviewed, CO, AZ, UT called</th>
<th>Physician information letter sent</th>
</tr>
</thead>
<tbody>
<tr>
<td>May 14</td>
<td>May 17</td>
<td>May 18</td>
<td>May 19</td>
<td>May 24</td>
</tr>
<tr>
<td>Notification sent to all states</td>
<td>Family and community contacts interviewed</td>
<td>CDC requested; Placitas meeting</td>
<td>CDC team arrives; Clinical conference</td>
<td>CDC: hantavirus antibody in 3 patients</td>
</tr>
<tr>
<td>May 25</td>
<td>May 26</td>
<td>May 27</td>
<td>May 29</td>
<td>June 4</td>
</tr>
</tbody>
</table>
Case History

- 15 y/o girl found dead at home
- Returned from 1 mo visit to Oklahoma 1 day earlier
- Rash on lower legs & cough
- Family discord
- Depressed- suicide attempt (ingestion Tylenol, iron) a few months earlier
Differential Diagnosis

- Infection (sepsis, plague, leptospirosis, RMSF)
- Leukemia
- Coagulopathy
- Toxin
Anticoagulant Poisoning

- Blood: 4-hydroxycoumarin
- “D-Con” (brodifacoum) & “Contrac” (bromadiolone) mouse poisons in house
- Metabolized to 4-hydroxycoumarin
- Long-acting anticoagulants - effect can last up to a year

Medicolegal Death Investigative System - Critical Element

- Recognizing fatal emerging infections & infections of public health importance
- Sorting out conditions which might mimic infections *i.e.* toxins
Forensic Pathology & Emerging Infections

- Plague - CA, 1919
- Malaria - IVDAs, NYC, 1933
- Plague - NM, 1970s
- West Nile encephalitis - NYC, 1999
Medical Examiner
Infectious Disease Deaths

- Infections 25% of natural disease autopsies*

- Pneumonia, meningitis, upper airway, encephalitis, myocarditis, necrotizing fasciitis, AIDS, sepsis

* Nolte KB, et. al., Arch Pathol Lab Med1996;1120:125-128
Public Health Surveillance

• Ongoing systematic collection, analysis & interpretation of outcome specific data
• Used in planning, implementation & evaluation of public health practice
• Prompt dissemination of results leads to action by those responsible for prevention and control
• Detect trends, outbreaks & epidemics
Surveillance - information for action.

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

Alexander Langmuir
NEJM, 1963; 268:182-191
Medicolegal Death Investigation Systems

• Medical Examiners (forensic pathologists) & Coroners
• Authorized by legislated state statute
• Investigate violent, sudden, suspicious, unexplained & unnatural deaths
• Determine: condition of body
  cause/manner of death
Forensic Autopsy

- Circumstances: scene, records, statements
- Physical autopsy
  - External & visceral exam
  - Histologic exam
- Laboratory tests: x-ray, toxicology, cultures, etc.
Death Certificates

- Permanent record of death
- Records cause & circumstances
- ICD coded- used to assess health of population
- Used to allocate services & resources
- Without autopsy, inaccuracy is limitation
ID Mortality Surveillance

- ID mortality increased 58% 1980-1992
- Due to HIV, respiratory infections, septicemia
- Together ID’s 3rd leading COD in US in 1992
- Limitation: Validity/accuracy of death certificates & ICD-9 codes

Syndromic Surveillance

- Uses non-specific manifestations or surrogates of target diseases that occur before diagnoses are routinely made
- Purpose: early recognition of disease or outbreak to allow intervention

*Sosin D. Biodefense Strategy Practice Sci 1:247-253, 2003*
Autopsy-based Surveillance: Advantages

- Enhanced diagnostic capacity with tissues
- Accurate determination of cause of death especially with infectious or toxic exposures
- Insights into pathogenesis or route of infection (HPS, inhalational anthrax)
- Rapid notification
- More infections recognized than encoded by death certificates (TB)
Advances in Pathologic Diagnosis of Infections

- Immunohistochemistry, *in-situ* hybridization, nucleic acid probes
- Fresh, frozen and formalin-fixed tissues (archived specimens)
Limitations of Medicolegal Death Investigation Systems

- Bias: violent deaths
- Satisfaction: general pathologic vs. organism-specific diagnoses
- Lack of access to sensitive modern diagnostic tests
Limitations of Autopsy

- No guarantee that organism will be identified
- Cultures: postmortem overgrowth & contamination
- EM: painstaking & dependent on tissue quality
- Serology: death precedes detectable immune response
Potential ID Death Recognition:
Limitations

• Most state statues similar
• Reporting notoriously incomplete: even for violent and traumatic deaths
• Investigators & pathologists may lack training to recognize potential infections
• Extent of investigation including autopsy varies by jurisdiction
• Result of pathologist availability, adequate facility, lab support ($)
Recognition of ID Deaths

- Ability of clinicians/police to identify & refer cases
- Level of training/experience of ME/Cs & investigators
- Quality of resources/facilities
- Ability to search autopsy records
- ME/C reporting to public health agencies
Biological Terrorism

The use or threatened use of biological agents or biologically-related toxins against civilians, with the objective of causing fear, illness, or death.*

*CDC
Medical Examiners/Coroners & Bioterrorism

• Investigate violent, suspicious, sudden, unexplained deaths including homicides & inapparent causes, *i.e.* drugs, toxins & infectious agents
• Respond to a known terrorist event
• Detect a covert attack (surveillance)
Response to a Known Terrorist Event

- Homicides - fall under ME/C jurisdiction
- Evidence (Murrah Bldg bombing)
- Mass disasters (aviation accidents, heat wave deaths)
- ME/Cs part of complex response team

Surveillance for a Covert Terrorist Attack

- ME/Cs might see sentinel fatalities
- Individuals with infections or poisoning might die at home
- Those hospitalized might die precipitously or unexpectedly without clear diagnosis
- Hantavirus pulmonary syndrome
- Cyanide contaminated acetaminophen

Public Health Preparedness & Response for Bioterrorism

- CDC - 1999
- NM Office of Medical Investigator & Department of Health
- B-2 - Special Surveillance Project
New Mexico
Office of the Medical Investigator

• Centralized, statewide, university-based
• 6 forensic pathologists
• 10 central and 130 field investigators
• Administers University Hospital autopsy service
• Trains fellows & pathology residents
New Mexico
Office of the Medical Investigator

- Investigates 4800 of 12400 deaths/year
- 1850 autopsies/year (>95% of NM autopsies)
- Sentinel groups*:
  - Children less than 2 years (7%)
  - Alcoholics (>7%)
  - IVDA’S (>5%)
  - AIDS patients (1.3%)

New Mexico
Office of the Medical Investigator

- Comprehensive autopsy report & computerized database
- Retrospective analyses/prospective coding for epidemiology & research
- Organization: statewide population-based surveillance
- UNM tie: consultation/collaboration, enhanced diagnostic accuracy, research
Med-X Surveillance

- Symptoms to capture potential cases
- Pathology-based syndromic reporting standards
- Organism & toxin specific diagnoses
- CDC - ID Pathology Activity - enhanced diagnostic capacity

Anthrax
Surveillance Symptoms to Accept Case for Autopsy

- Flu-like symptoms
- Fever & respiratory symptoms
- Acute encephalopathy or new onset seizures
- Descending paralysis, polyneuropathy
- New fatal rash
- New jaundice
- Acute bloody diarrhea w/o melena
- Unexpected death
Pathology-based Syndromic Surveillance

<table>
<thead>
<tr>
<th>Autopsy Syndrome</th>
<th>Potential BT Illness</th>
<th>Public Health Benefit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community-acquired pneumonia, Diffuse alveolar damage (ARDS)</td>
<td>Plague, tularemia, Q fever, inhaled staph enterotoxins B, clostridium, gil, other gases</td>
<td>Flu, pneumococcal &amp; other bacterial, viral pneumonias, HPS</td>
</tr>
<tr>
<td>Diffuse rash</td>
<td>Smallpox, VHF’s, T-2 mycotoxins</td>
<td>Varicella, measles, rickettsial, enterovirus, meningococcal infections, dengue, staph TSS</td>
</tr>
<tr>
<td>Sepsis syndromes i.e. DIC</td>
<td>Plague, tularemia, anthrax, VHF’s, T-2 mycotoxins</td>
<td>Gp A strep, meningococcal, pneumococcal, leptospiral, yellow fever, rickettsial infect.</td>
</tr>
<tr>
<td>Hemorrhagic mediastinitis or meningitis</td>
<td>Anthrax</td>
<td>Pulmonary leptospirosis &amp; H. simplex encephalitis</td>
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<tr>
<td>Encephalitis, meningitis</td>
<td>VEE and other equine encephalomyelitis agents</td>
<td>Viral, bacterial, fungal encephalitides &amp; meningitides</td>
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OMI Syndromic Surveillance

Investigator notified

Symptoms

Autopsy

Lab-specific Dx

No symptoms

No syndrome

No public health concern

No autopsy

DOH notified

Public health concern
Med-X Surveillance Data – 2 Years

- 250 (4.1%) of 6104 jurisdictional cases met entry criteria
- 141 (56%) had pathologic syndrome
Disease Categories

- Infectious disease 127 (51%)
- Toxin-related 31 (12%)
- Other 72 (29%)
- Undetermined 20 (8%)
Infectious Disease Deaths

Organism-specific diagnosis - 103 (81%) cases

– Notifiable conditions in NM - 60 (58%) cases
  • *S. pneumoniae* 37
  • *S. pyogenes* 8
  • *H. influenzae* 5
  • *M. tuberculosis* 1
  • Botulism 1
  • AIDS 2
Sensitivity and Specificity

- All symptoms for any syndrome
  - Sensitivity 86%
  - Specificity 97%
- Flu-like symptoms for pneumonia/DAD
  - Sensitivity 47%
  - Specificity 99%
- Fever + respiratory for pneumonia/DAD
  - Sensitivity 41%
  - Specificity 99%
### Predictive Value of Med-X Symptoms

<table>
<thead>
<tr>
<th></th>
<th>Number</th>
<th>Infectious Disease</th>
<th>Toxin</th>
<th>Other</th>
<th>Undetermined</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flu-like symptoms</td>
<td>95</td>
<td>62 (65%)</td>
<td>6 (6%)</td>
<td>26 (27%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Fever &amp; Respiratory</td>
<td>60</td>
<td>43 (72%)</td>
<td>4 (7%)</td>
<td>11 (18%)</td>
<td>2 (3%)</td>
</tr>
<tr>
<td>Unexpected Death</td>
<td>79</td>
<td>15 (19%)</td>
<td>12 (15%)</td>
<td>35 (44%)</td>
<td>17 (22%)</td>
</tr>
<tr>
<td>Encephalopathy or Seizures</td>
<td>25</td>
<td>13 (50%)</td>
<td>6 (23%)</td>
<td>6 (23%)</td>
<td>1 (4%)</td>
</tr>
</tbody>
</table>
Additional Cases

37 (15%) ordinarily no autopsy prior to criteria
- 1% increase in autopsy workload
- 21 (57%) had an infectious disease
  • 6 (29%) notifiable condition in NM
    - *S. pneumoniae* and *S. pyogenes*
Overall Timeliness

Mean: 29 days
Median: 6 days
Range: 0-468 days

Percent Reported

Interval From Death to DOH Report (weeks)

1 2 3 4 >4

Percent

0.0 10.0 20.0 30.0 40.0 50.0 60.0

53.8 15.9 2.8 2.1 25.5
Timeliness: Gross vs Microscopic

Gross
Average: 18 days
Range: 0-468 days

Microscopic
Average: 54 days
Range: 5-384 days

Percent Reported

Weeks
Timeliness: Problems

- Confusion over data entry
- Missed cases entered retrospectively
- Delay for histology preparation & review
- Tardiness
ME Surveillance: Conclusions

• Flu-like symptoms, fever & respiratory symptoms, and encephalopathy/new-onset seizures highly predictive of infections
• Sudden unexpected death less likely to represent an infection
• Organism-specific diagnoses are possible in the majority of ID deaths
ME Surveillance: Conclusions

• Uniform autopsy & reporting criteria increase recognition of PH conditions & likelihood of recognizing bioterrorism deaths
• Timely reporting is possible
• Combined surveillance systems serve the public good & can be tested, modified, utilized daily
Public Health Implications

- ID mortality is fraction of ID occurrence
- Fatalities can portend greater morbidity
- Category A agents- substantial mortality
- Fatality recognition impt to understand outbreak scope
- PH officials need to review mortality & morbidity surveillance data
Requirements to Distribute Med-X

- Uniform jurisdiction within a defined area
- Uniform investigation of jurisdictional deaths
- Access to diagnostic laboratory
- Electronic data management system
- Linkage to a health department sharing the same jurisdiction
- Currently being implemented in NH, OR, WI, LA
Med-X Distribution: Impediments

- Funding
- Organizational location of agency
- Biosafety
Let conversation cease, 
let laughter flee, 
for this is the place where 
death delights to help the living.
# Partners

<table>
<thead>
<tr>
<th><strong>OMI</strong></th>
<th><strong>NM Dept of Health</strong></th>
<th><strong>CDC</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Sarah Lathrop</td>
<td>Maggi Gallaher</td>
<td>Sherif Zaki</td>
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<tr>
<td>Georgine Durka</td>
<td>Stuart Castle</td>
<td>Wun-Ju Shieh</td>
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<tr>
<td>Jim Perrings</td>
<td>Edith Umland</td>
<td>Jeannette Guarner</td>
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<tr>
<td>Marcus Nashelsky</td>
<td>Jennifer Downey</td>
<td></td>
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<tr>
<td>Jerri McLemore</td>
<td>Joan Baumbach</td>
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<tr>
<td>Jeffrey Nine</td>
<td>Bernadette Albanese</td>
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<td>Rebecca Irvine</td>
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<td>Barbara Bollinger</td>
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<tr>
<td>Patricia McFeeley</td>
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<tr>
<td>Ross Reichard</td>
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<tr>
<td>Ross Zumwalt</td>
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Med-X Surveillance Symptoms

- Flu-like symptoms (fever or chills or myalgias)
- Fever and respiratory symptoms (cough or shortness of breath or chest pain or hemoptysis)
- Encephalopathy (acute mental status change with or without other neurologic symptoms) or new-onset seizures
- Descending paralysis, polyneuropathy
- New fatal rash
- New jaundice
- Acute bloody diarrhea without melena
- Unexpected death (where the circumstances, past medical history and scene investigation provide inadequate diagnostic insight to establish the cause of death) of an individual less than 50 years of age without any of the other above symptoms.
## Med-X Surveillance Pathologic Syndromes

<table>
<thead>
<tr>
<th>Autopsy-based pathologic syndrome</th>
<th>Potential bioterrorism illness</th>
<th>Other infections of public health importance</th>
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<tr>
<td>Community-acquired pneumonia, diffuse alveolar damage</td>
<td>Plague, tularemia, Q fever, inhaled staphylococcal enterotoxin B, ricin, phosgene, chlorine &amp; other gases</td>
<td>Influenza, hantavirus pulmonary syndrome, pneumococcal and other bacterial &amp; viral pneumonias</td>
</tr>
<tr>
<td>Bronchitis, bronchiolitis</td>
<td>Q fever</td>
<td>Influenza, RSV infection</td>
</tr>
<tr>
<td>Pharyngitis, epiglottitis and other upper airway infections</td>
<td>Viral hemorrhagic fever (Lassa)</td>
<td><em>H. influenzae, Diphtheria</em> infections</td>
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<tr>
<td>Soft tissue infections- (cellulitis, necrotizing fasciitis, abscess)</td>
<td>Anthrax</td>
<td>Group A Streptococcus</td>
</tr>
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<td>Sepsis syndromes e.g., disseminated intravascular coagulopathy</td>
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<td>Myocarditis</td>
<td>Q fever</td>
<td>Enterovirus, influenza, adenovirus &amp; other viral infections</td>
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<tr>
<td>Hepatitis, fulminant hepatic necrosis</td>
<td>Brucellosis, viral hemorrhagic fevers</td>
<td>Viral hepatitis, dengue, leptospirosis, yellow fever, ECHO virus hepatotoxins</td>
</tr>
<tr>
<td>Hemorrhagic colitis</td>
<td><em>C. perfringens, E. coli</em> and <em>Shigella</em> colitis, Anthrax</td>
<td><em>E. coli</em> and <em>Shigella</em> colitis</td>
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February 12, 2006

Reference List


