

## Response to a Covert Chemical Threat

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## Challenging Preparedness: Mass Poisoning in Maine

- Scope – a broad poison center perspective
- Scale and rural character of the region
- Strength = Weakness
  - Danger = Opportunity
- The Northern New England Poison Center
  - Maine and Vermont
  - Balanced for scale: hotline services and outreach
  - Hospital, federal, state, private partnerships and funding

## Some Roles of the NNEPC in emergency preparedness and response:

- 24- hour hotline for exposures and information
  - Surveillance
  - Notification of relevant prevention and response agencies
- Toxicology consultations
- Public/professional outreach & risk communications
- Scholarly activity
- Antidote registry for hospital supplies – minimizes cost & transport time, optimizes availability of unusual antidotes
- Maine Hospital Pharmacy Antidote Stockpile:
  - 1997 through 9-11-2001 and into the future
- Bureau of Health "After Hours On Call" contract

## History, Geography and Onset

- **Saturday, April 26<sup>th</sup>** - Bake sale, New Sweden, Maine church group. Food (baked goods & sandwiches) donated by church members. Leftovers saved.
- **Sunday, April 27<sup>th</sup>** – Some after church coffee hour attendees become ill during the hour and worsen progressively afterward. Time to onset of symptoms is initially unclear.



## The Syndrome and Presentation

- 3:30 pm– 9:35 pm: Some attendees from church coffee hour present to Cary Medical Center with nausea & vomiting. A few also had diarrhea, and fewer had hypotension.
- 12/16 came to the Emergency Department
  - 3 later transferred to Eastern Maine Medical Center
  - 5 seen and released
  - 4 admitted to CMC



## The incoming calls... first

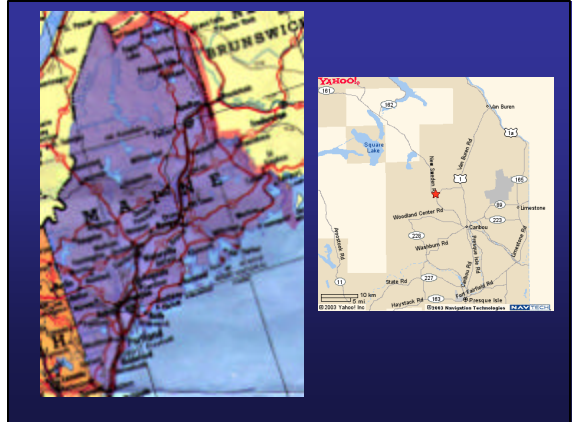
- 6:58 pm : State Bureau of Health AHOC Hotline - CMC requests epi assistance with an outbreak of infectious disease or food-related illness
  - On-Call contact paged; begins collection of data, notifies State Epidemiologist. Extensive plans to include epidemiologist and sanitarian for on-site investigation in AM.
  - Staph enterotoxin, scombroid, well water??



## and then...



- 7:38 PM: CMC ICP calls NNEPC Staff on the Poison Center Hotline for info to expand the working differential diagnosis to include toxins.
- One patient is in ICU with 'sepsis'
  - NNEPC Staff reviews toxicologic differential diagnosis consistent with the syndrome and requests that all beverages and foods potentially linked to the illness be secured for investigation.



## Follow-up calls



- 10:15 pm: State calls CMC, no new information at this time. To contact epi on-call if any changes.
- 10:20 pm: NNEPC contacts CMC for follow-up. Receives general patient information. BOH will come in the morning to retrieve specimens for testing.
- Late evening: 3 patients from CMC are transferred to EMMC because of hypotension.

## Monday, April 28<sup>th</sup>

- **Early morning:** 78 year old male with history of a recent major cardiac event dies at CMC.
- **3:35 am:** EMMC requests MD tox consult. NNEPC staff discusses differential & both toxicologists are consulted. Both suggest:
  - Heavy metal poisoning (likely arsenic, less likely antimony, or lead based on time course)
  - Unlikely paraquat, diquat, ricin or thallium
  - Advise clinical samples (emesis, blood, urine) be sent to HETL for analysis

## As this is ongoing...

- Perform continuous "Maine-based reality check"...
- Is mass poisoning with arsenic a real possibility in New Sweden?
- Are there any other outbreaks??



Cary Medical Center  
65 beds

Eastern Maine Medical Center  
411 beds



Maine Medical Center  
606 beds

Ongoing NNEPC consults support CMC & EMMC clinicians

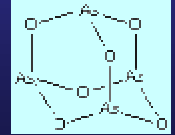
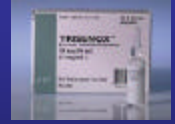
## Poison Center AM Actions

- ~ 07:30 - Confirmation of lab staff readiness to run metals, pesticides and other organics in real-time
  - Awaiting expedited transfer of samples
- ~ 08:00-10:00 – Participate in discussion with CMC, EMMC, BoH, State Police, Medical Examiner and other state officials mobilizes statewide resources and investigation
  - Chain of custody discussed for clinicians
  - Follow-up conference times set
  - HAZMAT etiologies considered
  - Forensic evidence secured
- Begin mobilization of MMC and other hospital antidote stores in addition to new Maine Hospital Pharmaceutical Stockpile antidotes for use in the event that arsenic is confirmed
- Consult with law enforcement re: potential poisons

## Arsenic Trioxide: A Pharmaceutical

### •Side Effects when used to treat Acute Promyelocytic Leukemia

- leukocytosis
- hyperglycemia
- dyspnea
- cough
- rash or itching
- headaches
- edema
- dizziness
- nausea
- vomiting
- diarrhea
- abdominal pain
- fatigue



...and don't forget melarsoprol for trypanosomiasis!

## Arsenic as a poison...

- Shock – mimics SIRS
- Arrhythmias & prolonged QTc
- Cardiac dysfunction
- Pulmonary edema/ARDS
- Rhabdomyolysis
- Renal failure
- Liver failure / hepatitis
- Hemolytic anemia
- Neuropathies
- Altered mental status and seizures

## Arsenic Exposures

- Organic
  - Arsenobetaine
  - Arsenocholine
- Inorganic
  - Tasteless & odorless
  - ? absorption if dissolved
  - Poor absptn. thru skin
- Acute
- Chronic
  - 50 ppb in water associated with bladder and lung CA
  - U.S. level now 10 ppb
- Often only detected post-mortem.

## Arsenic Clearance

- Three phases:
  - 1. 2-3 hours - more than 90% clearance
    - $t_{1/2} = 1-2$  hrs
  - 2. 3 hrs – 7 d – slow decline; As:plasma::3:1
    - $t_{1/2} = 30$ hrs
  - 3. 10 d or more – estimated  $t_{1/2} = 300$  hours

## Other As facts...

- Interconversion of  $As^{+5}$  (arsenate) and  $As^{+3}$  (arsenite) is reversible
- Potential targets: brain, RBCs, with interconversion in liver, testes, kidneys and lungs
- Crosses placenta
- Not appreciable secreted in breast milk
- Estimated  $LD_{50}$  (for humans in mg/kg):
  - $As_2O_3 = 1.43$ ; MMA = 50; DMA = 500

## Molecular Targets of As

- SH groups of many enzymes and substrates
  - Dihydropyrimidinone (pyr ? Acetyl Co A and a-KG ? succ Co A)
  - Thiolase
  - Glutathione synthetase and glutathione reductase
  - G-6-PDH
  - Multiple mechanisms proposed for induction of CA

## Treatment - Supportive care +

Agent	Pro	Con
BAL	Known efficacy, intra & extracellular, IM injection (overcomes GI dysfunction)	pain, toxic, peanut oil, ?BP, N, V, HA, ?T, hemolysis (G-6-PDH), ? trace metals, ? brain & testes As
DMSA	Protects from lethality, oral	N, V, D, Abd. pain, extracellular, ? LFTs, rash, pruritus, paresthesias, ? PLT and eos
DMPS	IV, IM or oral, extra & some intracellular action	Allergy, N, Pruritus, vertigo, weakness, ? trace metals, not FDA approved

## Poison Center Actions ~ Midday

- NNEPC staff handle daily volume while mobilizing antidotes and providing arsenic-specific information to clinicians
  - Request that CMC & EMMC pharmacies order additional supplies from vendors for day 2.
  - Couriers, State Police and a plane transferring a critically ill patient distribute the initial antidote supplies.
- CMC and EMMC cases remain open pending pertinent data, follow-up and time for computer entry.
- NNEPC discusses differential diagnosis with other toxicologists – differential supported without addition.
- NNEPC cases automatically uploaded to the American Association of Poison Control Centers' (AAPCC) Toxic Exposure Surveillance System in Washington, D.C.

## Rapid Recognition

- Gastroenteritis-like illnesses of unusually rapid onset and severity
- Apparent exposure to contaminated food
- Small community: patients report to a single source of medical care
- Cluster is recognized and reported
- Toxicologists are consulted and recognize the toxidrome

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## An Act of...

- Intentional mass poisoning, with the suspected aim of affecting church policy
- Terrorism: The premeditated threatened or unlawful use of force or violence by an individual person or an organized group against non-combatant people or property with the intention of intimidating or coercing societies or governments, often for ideological, religious or political reasons.

## Poison Center Surveillance

- TESS surveillance flags trip for call volume, hypotension & tachycardia as staff enter data.
- AAPCC calls NNEPC to investigate the sudden increase in exposures via Bill Watson.
- AAPCC notifies the Centers for Disease Control and Prevention and the Department of Homeland Security.
- Differential diagnosis re-confirmed with AAPCC.

## Epidemiologic Concerns

- Protection of Public Health
- Traditional epi investigation points to the coffee
- Was the etiologic agent included
  - on site?
  - after shipping from the manufacturer?
  - before packaging?
  - before importation?
- Is it contagious?



## Forensic Concerns (from the poison center perspective)

- Protection of individual and public health; support for law enforcement investigation
- Rapid clinical response to minimize morbidity and mortality
- Collection of all available evidence for fastest identification of the etiologic agent
  - Including food, beverages, body fluids for unknown biological and toxic agents...
- Protecting the integrity of that evidence
  - Including chain of custody, correct sampling procedures, sample integrity...

## Confirmation: **Monday, April 28**

- **5 PM- 6:15 PM:** Samples arrive at HETL from CMC, EMMC and New Sweden
- **~7:45 PM:** Notified that first blood sample run is positive for As; coffee sample is also positive for As
- EMMC and CMC are called via NNEPC-- patient care instructions:
  - EMMC: BAL for all (critically ill); 5 total transferred pts.
  - CMC: BAL (onsite) for all, followed by DMSA when available for those able to tolerate oral therapy.
  - Discharged patients with lesser symptoms + those not previously seen are recalled for treatment.

## Case Evolution 1



- Several patients had lifethreatening toxicity and required intensive care for days to weeks. Some have arrhythmias resulting from arsenic exposure. None had developed neuropathies at last follow-up.
- The treatment of these patients was complicated by severe respiratory distress, renal dysfunction and failure, rashes and liver injury.
- NNEPC sets up database to follow clinical effects and labs.
- Medical toxicologist consults provided via telephone and on-site at CMC and EMMC
  - The most gravely ill were treated with an IV antidote not fully FDA approved
- Therapy for the patients was not interrupted due to antidote shortage.

## Case Evolution 2

- NNEPC provides antidote administration and dosing guidelines to treating clinicians. Staff and Toxicologists discuss expected course.
- During following weeks: consultations between the NNEPC Staff/Toxicologists & treating hospitals often occurred several times daily. Untold hundreds of calls were placed in consultation and follow-up to:
  - Optimize patient care given complex problems and available resources
  - Address concerns of patients and families
  - Assist in provision of information for news media
    - Toxicologists provide over 20 interviews discussing arsenic toxicity
    - Use opportunity to raise awareness of unrelated (but regionally significant) chronic arsenic exposure through well water
  - Select strategies for long term inpatient care, discharge planning and outpatient follow-up
  - Assist in selection and monitoring of laboratory studies

## Additional tasks for NNEPC

- Multiple on-site visits with patients and families; extensive follow-up
- Develop informational fact sheets for patients & families to explain the effects of acute arsenic poisoning
- Consults regarding emergency use of unapproved drugs
- Develop informational materials for the treating professionals to explain therapy to patients and facilitate DMPS consent
- Provide insurance companies with information supporting length of stay, use of non-FDA approved drug
- Develop discharge and outpatient care criteria
- Facilitate experimental investigation of contaminated dentures
  - significant amounts of arsenic had been retained in some dentures and was later released in artificial saliva surrounding the dentures
- Police consult with NNEPC toxicologists several times during investigation regarding testing of samples, arsenic levels and sources.

## Influence on NNEPC Utilization

- During this time, the Poison Center continued to manage approximately 100 other hotline calls daily.
- The publicity surrounding these cases increased unusual (time intensive) consultations with questions about food poisoning or potential chronic heavy metal exposures.

## Lessons Learned or Confirmed - 1

- Awareness of potential for chemical events and their long-term consequences must be raised.
- Awareness of laboratory capabilities is pivotal.
- Vendor Managed Inventory is not adequate for early treatment in large states without vendors.
  - Antidote registries and stockpiles are crucial in early hours.
- Planning, knowledge of local resources & constraints, travel times, levels of care available by facility, contribute to improved patient care.



## Lessons Learned or Confirmed - 2

- Prior NNEPC connectivity with the individuals & organizations needed to facilitate care saved time.
- Prior Poison Center outreach to the health care professionals and institutions involved allowed them to use toxicology experts efficiently and with confidence, especially considering the unusual nature of necessary interventions recommended by NNEPC.
- Improved poison center funding will allow staffing to meet surveillance demands and emergency priorities.
- **The test: the next arsenic poisonings in our region**

## Rapid Response

- Prepare to act in real-time (even after hours) to minimize the need to “get up to speed” after an event.
  - Remain “in-phase” with the ICS and other incident managers from the start.
- Labs have been fundamental to public health practice.
  - New emphasis is needed on chemistries.

## Benefits Realized from Homeland Defense-Related Funding

- Contract between NNEPC and BoH to improve After Hours On-Call System, provide professional case triage and capture related data
- Funds for Maine Hospital Pharmaceutical Stockpile, to include BAL not widely stocked
- Improved State Laboratory capacity and procedures
- Regional epidemiologist presence, new in Maine
- Conference Call system - anywhere, anytime
- HAN used to inform other hospitals of the outbreak

## Clinical System Stressors

- CMC & EMMC:
  - ED, Critical Care and other areas stressed by patient volume at initial presentation or when recalled for care; security needs; news media; financial; mental health needs; more
  - Hospital Labs overloaded by high volume of requests for unusual labs, chain of custody, and 'send out' samples
- NNEPC: Demand for initial diagnostic, supportive and definitive care was high & delayed case entry into TESS; time-consuming long-term care needs for staff & toxicologist resources persist for weeks & are superimposed on brisk daily volume
- Staffing and other resources are generally fixed

## The relevance of all this?

- It's not just about arsenic...
- It's not just about toxicology...
- It IS about assessment, planning, preparing and communication, and
- it's mostly about TEAMWORK!

## Acknowledgements

- The staff of the Northern New England Poison Center, Maine Medical Center and our other private grantors
- Cary Medical Center
- Eastern Maine Medical Center
- The State of Maine, the Maine Bureau of Health and Maine's Health and Environmental Testing Laboratory
- The Centers for Disease Control and Prevention
- The Health Resources and Services Administration
- The American Association of Poison Control Centers
- And many others including Maine's EMA and Public Safety Agencies



## A Parting Thought

- “Never doubt that a small group of thoughtful, committed citizens can change the world.”

– Margaret Mead (1902-1978)