Chemical Agents of Opportunity for Terrorism: TICs & TIMs

Module Two
The Clinical Neurotoxicology of Chemical Terrorism

Training Support Package
Goals and Objectives

- Recognize toxic syndromes that effect the nervous system
  - Sedation
  - Convulsions
  - Hallucinations
- Know unique clinical effects of toxins that cause sedation syndromes
- List examples of agents of opportunity for each syndrome
- Know initial treatment strategy
Central Nervous System

• The CNS is immensely complex
  – Great target for terrorism
• The CNS is central to both our function and our thinking
The Balance of the Brain

- The brain is a fine balance of excitatory and inhibitory influences
  - Slight alterations in either direction are significant

Excitation

Inhibition

Glutamate
Catecholamines

Gamma-aminobutyric acid (GABA)
The Balance of the Brain

• In addition, other neurotransmitters influence our mood, our ability to think, remember, etc.

Modulators of Thought Processes
Serotonin
Acetylcholine
Clinical Syndromes of the CNS

Too much inhibition = Sedation/coma
Clinical Syndromes of the CNS

Too much stimulation = Convulsions
Clinical Syndromes of the CNS

Altered Modulation of Thoughts = Hallucinations
Clinical Syndrome: Sedation

- Excitation
- Inhibition
Ethanol Intoxication: A Prototype for Calmatives

- Dose-Response
  - The more you drink, the drunker you get
  - 1 beer: buzz
  - 2 beers: intoxicated
  - 6 beers: uncoordinated, slurred speech,
    - Disinhibited
  - 24 beers: coma, respiratory arrest
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Case Study: Moscow Theatre Hostage Crisis (2002)
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Case Study: Moscow Theatre Hostage Crisis (2002)
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- Russian Federal Security Service pumped unidentified “gas” into building
- Security forces raided building
- 128 of 800 (16%) hostages died
  - All but one from gas
- All 42 separatists died
  - 39-41 from gas
What happened?
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Mike Hanna: Russia won’t reveal gas used in rescue

MOSCOW, Russia (CNN) -- The vast majority of deaths in a hostage standoff at a Moscow theater appear to have been caused by a sedative gas used to subdue the hostage takers, Russia's chief medical examiner said Sunday.

Of the 117 hostages who died, 115 apparently died from the gas, and more than 100 people who survived.

Lethal Moscow Gas An Opiate?

BOSTON, Oct. 29, 2002

(CBS) The lethal gas that killed 116 Moscow theater hostages may be an opiate related to morphine, U.S. officials said Monday.

Such substances not only kill pain and dull the senses but also can cause coma and death by shutting down breathing and circulation.

Doctors from a Western embassy examined some of the former hostages and concluded the agent they were exposed to appears consistent with an

Russia names Moscow siege gas

MOSCOW, Russia (CNN) -- Four days after Russian forces used anesthetic gas to end a hostage standoff by Chechen rebels, Russia’s top health official identified the main component of the gas blamed for the deaths of 117 hostages.

The gas was based on derivatives of fentanyl. Health Minister Yuri Shevchenko said Wednesday.

Fentanyl is an opiate-based narcotic 100
### Characteristics of Opioids

<table>
<thead>
<tr>
<th>Agent</th>
<th>Potency (vs. morphine)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>1</td>
</tr>
<tr>
<td>Meperidine</td>
<td>0.5</td>
</tr>
<tr>
<td>Methadone</td>
<td>4</td>
</tr>
<tr>
<td><strong>Fentanyl</strong></td>
<td><strong>300</strong></td>
</tr>
<tr>
<td>Sufentanil</td>
<td>4500</td>
</tr>
<tr>
<td>Alfentanil</td>
<td>75</td>
</tr>
<tr>
<td>Remifentanil</td>
<td>220</td>
</tr>
<tr>
<td><strong>Carfentanil</strong></td>
<td><strong>10,000</strong></td>
</tr>
</tbody>
</table>

Chemical Agents of Opportunity for Terrorism: TICs & TIMs

WILDLNIL®

**Product Description**
An extremely potent opiate anesthetic used for rapid immobilization of free-ranging and captive members of Cervidae. Formulated at 4.46% mg/ml Carfentanil Citrate, WILDLNIL produces rapid immobilization following intramuscular injection.

**Section 2 Hazardous Ingredients/Identity Information**

<table>
<thead>
<tr>
<th>Hazard Components</th>
<th>CAS #</th>
<th>% by Wt</th>
<th>ACGIH TLV</th>
<th>OSHA PEL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carfentanil Citrate</td>
<td>61380-27-6</td>
<td>0.45</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td>Sodium Chloride</td>
<td>7647-14-5</td>
<td>0.80</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Sterile Water for Injection</td>
<td>7732-18-5</td>
<td>98.55</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

**Section 3 Physical/Chemical Characteristics**

- **Appearance:** Clear Liquid
- **Boiling Point:** 100 °C
- **pH:** 3.0-4.5
- **Odor:** None
- **Specific Gravity:** 1.023
- **Vapor Pressure:** 23.756 mmHg @ 25°C
- **Water Solubility:** Completely Soluble

[Module Two - The Clinical Neurotoxicology of Chemical Terrorism](#)
Positive Purpose

“The use of pharmacological agents to produce calm behavioral state, particularly as relevant to management of individuals and/or groups that are agitated, aggressive and/or violent, is a topic with high relevance to achieving the mission of law enforcement and military communities”

(nldt2.arl.psu.edu/documents/calamative_report.pdf)
Inhaled Calmatives/Sedatives

• Aerosolized drugs
  – GABAergic agents
    • Benzodiazepine (e.g. diazepam)
    • Barbiturate (e.g. pentobarbital)
  – Opioids

• Volatile agents
  – Hydrocarbons
Calmatives/Sedatives

- Suspect whenever clinical picture presents with predominant CNS depression
  - All produce dose dependent sedation
- Major complication: RESPIRATORY DEPRESSION
  - Respiratory depressant effects vary
- Specific Toxic Syndrome: CNS depression, pinpoint pupils, and respiratory depression = Opioid
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Rapid Recognition leads to Urgent Intervention

Miosis
CNS Depression
Respiratory Depression

Narcan 0.4mg/mL
Naloxone HCl Injection, USP
Treatment strategy

Excitation
Inhibition

Naloxone

Excitation
Inhibition
Management of Calmative / Sedative Poisoning

- Supportive care
- Antidotes for several are available
  - Of limited utility
Audience Response

What is the most important treatment for patients who have respiratory depression?

1. Artificial ventilation
2. Chest compressions
3. Naloxone
4. Oxygen
What is the most important treatment for patients who have respiratory depression?

1. Artificial ventilation
2. Chest compressions
3. Naloxone
4. Oxygen
5.
6.
7.
8.
9.
10.
Clinical Syndrome: Convulsions
Convulsions

• The brain is a fine balance of excitatory and inhibitory influences
  – Slight alterations in either direction are significant
• “Inhibition of inhibition” is the most common cause of drug induced seizure
Inhibition of inhibition
Poisoning by an Illegally Imported Chinese Rodenticide Containing Tetramethylenedisulfotetramine — New York City, 2002

Illegally imported foreign products can result in domestic exposures to unusual toxic chemicals, and health-care providers might not be able to provide appropriate therapy because the chemical ingredients might not be listed or recognized even after translation of the product label. This report describes the first known case in the United States of exposure to a Chinese rodenticide containing the toxin tetramethylenedisulfotetramine (TETS), a convulsant poison. The report of this investigation highlights the need to prevent such poisonings through increased public education, awareness, and enforcement of laws banning the importation of illegal toxic chemicals.

On May 15, 2002, a previously healthy female infant aged 15 months living with her family in New York City was found by her parents to be playing with a white rodenticide powder that they had brought from China and applied in the corner of their kitchen. After 15 minutes, the child had generalized seizures and was taken to an emergency department. Her initial blood glucose level was 108 mg/dL (normal range: 80–120 mg/dL). Despite aggressive therapy with lorazepam, phenobarbital, and pyridoxine, she had intermittent generalized seizure activity for 4 hours and required intubation. After her death, forensic toxicology revealed a fatal dose of TETS. This product was labeled as a food additive, a fertilizer, and a household cleaner.
Man Admits Poisoning Food in Rival’s Shop, Killing 38 in China

By ERIK ECKHOFF

BEIJING, Sept. 17 — A jealous business rival has confessed to spiking the food in a snack shop in a suburb of China, with rat poison, killing 38 people, mostly schoolchildren, and sending hundreds more to the hospital, state news organizations reported tonight.

Emulating a two-day massacre in an official report about the poisoning in Sept. 14, China Central Television and the New China News Agency said this evening that a man named Chen Zhaoping had admitted to placing a poison rat poison in products of the Zhangzhu Pantry to Taohua, a town near the city of Nanjing in Jiangsu Province.

Signaling school students and others who relied on the shop for breakfast, he expanded his operation after eating fried dough sticks, sesame cakes and sticky rice balls on Saturday morning. Some pupils collapsed right in front of the shop, blinking from the smoke and gas, witnesses said.

The accussed man ran a rival shop and told the police that “he carried a hatred because of business competition,” according to a television report.

By some accounts, Mr. Chen simply hoped to make patrons ill when he placed the poison — a banned pesticide called Deleatty — in the rival store’s products.

But when people started dying, he fled and was arrested Sunday in Shanghai, 374 miles to the north, officials said. He has been transferred to Nanjing, and investigation of the case continues, the police said.

Unconfirmed reports from a Hong Kong newspaper said his. Chen was a cousin of the owner of the shop whose food was poisoned, who by various accounts is in custody or in the hospital.

Deleatty contains sibutramine, a chemical that attacks the nervous system, and was banned in 1981, officials said. But illegal production has continued in the countryside, and the poison has been used in other crimes, as well as in many suicides.

As early, sketchy accounts of the mass poisoning, China’s controlled news outlets said virtually nothing about the case over the last few days, spawning rampant speculation and conflicting accounts of the toll. Reports in some papers here and in Hong Kong have quoted unidentified Zhangzhu officials as saying that 48 or more had died and hundreds more were seriously ill.

Tonight’s official report said 38 were dead, and 6 others were in critical condition, while “most of the 200 victims” were in stable condition.

Personal grudges have been blamed for several bombings and poisoning attacks in China in recent years, but the toll this time was unusually high.
Tetramine

• Du-shu-quiang ("very strong poison")
• Used as a rodenticide in China
  – Banned in 1984
• Like many substances used as rodenticides, tetramine is highly toxic to humans
Rat Poison

61 students felled by rat poison in central China

BEIJING, Sept. 29 (Xinhuanet) -- Dozens of elementary school students and teachers in Hunan Province were hospitalized after ingesting rat poison with their school breakfasts in an apparent deliberate mass poisoning, state media said Sunday.

Sixty-one students from the Changhu Township Center Elementary School were in a hospital in the city of Yueyang, 23 of them in critical condition, said a city spokesman.

Investigators believe poison was deliberately placed in school food but don't have any suspects yet, said the spokesman.

All 317 students and staff who ate breakfast at the school on September 23 were sent to hospitals for checkups after their classmates and colleagues began vomiting and fainting, the Beijing Times newspaper said. People who ate the breakfast complained of head and stomach aches, it said.
Some Chemical Causes of Convulsions

- Organophosphate & Carbamate Insecticides
- Nicotine
- Hydrazines
- Camphor
- Organochlorines
- Strychnine
Convulsions: Management

- Benzodiazepines
- Barbiturates, propofol
- Pyridoxine
  - Empiric dose, 5 gms (70 mg/kg)
“Playing with Our Mind”
Hallucinogens

- Alter modulation of thought processes
  - Serotonergic
  - Sympathomimetic
  - Anticholinergic
  - Anesthetic (PCP and ketamine)
Serotonergic Hallucinogens

- LSD
- Tryptamines (DMT, 5-MeO-DMT, psilocybin)
- Ololiuqui (morning glory seeds)
Serotonergic Hallucinogens

- 1968 - The Yippies (Youth International Party)
- Threatened to “space-out” or “turn on” the delegates to the Democratic National Convention in Chicago, and everyone else in Chicago as well, by dumping LSD into Lake Michigan.
Anticholinergic Hallucinogens

Atropine, Scopolamine and Hyoscyamine
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Clinical Effects

• Mad as a hatter
• Red as a beet
• Dry as a bone
• Hot as Hare
• Blind as a bat
• Full as a flask
(Also decreased GI motility)
Modern History

- 1676: a group of men led by Captain John Smith were sent to Jamestown, Virginia to quell the Bacon rebellion.

- Gathered the plant now known as “Jamestown weed” (or Jimsonweed), *Datura stramonium*, for a salad.
Bacon Rebellion

1676, Bacon Rebellion:

The soldiers presented a “very pleasant comedy, for they turned natural fools upon it for several days: one would blow a feather in the air; another would dart straws at it with much fury; and another, stark naked, was sitting up in a corner like a monkey, grinning and making mows at them….. A thousand such simple tricks they played, and after 11 days returned themselves again, not remembering anything that had passed.”

Robert Beverly, The History and Present State of Virginia (1705)
July 1995
Bosniaks fleeing Srebrenica during the war in Bosnia and Hercegovina.

“Survivors gave consistent descriptions of mortar shells that produced a ‘strange smoke’ of various colors which did not rise but spread out slowly. Following these attacks, some of the marchers - the numbers are unclear - began to hallucinate and behave in an irrational manner with some even killing their friends or themselves. . . .”

Human Rights Watch

**BZ: 3-Quinuclidinyl benzilate (QNB)**

Anticholinergic Hallucinogens

- Qualitatively similar

<table>
<thead>
<tr>
<th></th>
<th>Atropine</th>
<th>Scopolamine</th>
<th>BZ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose (70 kg)</td>
<td>8-14 mg</td>
<td>2 mg</td>
<td>0.5 mg</td>
</tr>
<tr>
<td>Duration</td>
<td>4-8 h</td>
<td>2-4 h</td>
<td>48-72 h</td>
</tr>
</tbody>
</table>
Treatment strategy
Concluding Thoughts

- The CNS is a unique target organ for terrorism
- Limited number of acute clinical consequences
- Management is generally symptomatic although “antidotes” may be available for certain agents.
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Questions?

Training Support Package