



Chemical Agents of Opportunity for Terrorism: TICs & TIMs

Module Two
The Clinical Neurotoxicology of Chemical Terrorism

Training Support Package

1



Chemical Agents of Opportunity for Terrorism: TICs & TIMs

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

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Chemical Agents of Opportunity for Terrorism: TICs & TIMs

Central Nervous System

- The CNS is immensely complex
 - Great target for terrorism
- The CNS is central to both our function and our thinking



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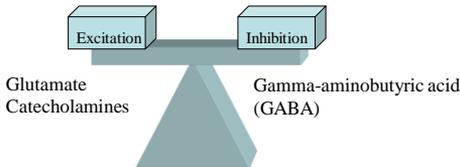
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Chemical Agents of Opportunity for Terrorism: TICs & TIMs

The Balance of the Brain

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



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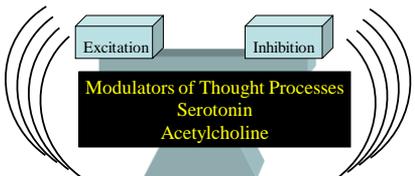
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Chemical Agents of Opportunity for Terrorism: TICs & TIMs

The Balance of the Brain

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



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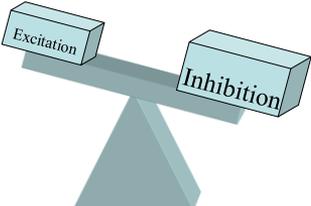
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Chemical Agents of Opportunity for Terrorism: TICs & TIMs

Clinical Syndromes of the CNS

Too much inhibition = Sedation/coma



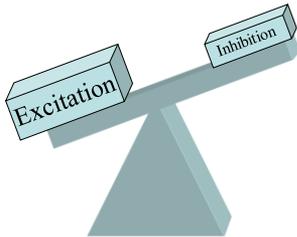
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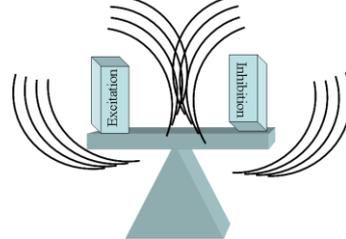
Clinical Syndromes of the CNS

Too much stimulation = Convulsions

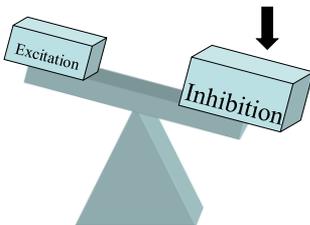


Clinical Syndromes of the CNS

Altered Modulation of Thoughts = Hallucinations



Clinical Syndrome: Sedation



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



Case Study: Moscow Theatre Hostage Crisis (2002)



Case Study: Moscow Theatre Hostage Crisis (2002)





Case Study: Moscow Theatre Hostage Crisis (2002)

- 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?



Mike Hanna: Russia won't reveal gas used in rescue

Sunday, October 27, 2002 Posted: 1:46 PM EST (1946 GMT)

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.



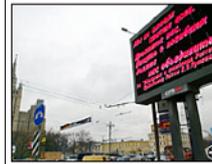
CNN's Mike Hanna

Of the 117 hostages who died, 115 apparently died from the gas, and more than 800 people who survived



Lethal Moscow Gas An Opiate?

MOSCOW, Oct. 29, 2002



A Moscow billboard displays President Putin's words on the deaths in the theater: "We could not save everyone. Forgive us. Memory of those killed should help unite us."

(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

Wednesday, October 30, 2002 Posted: 9:11 PM EST (0211 GMT)

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



Fentanyl is a potent narcotic used for anesthesia.



Characteristics of Opioids

Agent	Potency (vs. morphine)
Morphine	1
Meperidine	0.5
Methodone	4
Fentanyl	300
Sufentanil	4500
Alfentanil	75
Remifentani	220
Carfentanil	10,000

Wax PM, Becker CE, Curry SC. Ann Emerg Med 2003;41:700-5.

Wildlife Pharmaceuticals MATERIAL SAFETY DATA SHEET
 1402 Cliff Drive, Suite 600
 Fort Collins, CO 80524
 (970) 494-6267
 January 3, 2000

Section 1 Identification

Product Name: Wildnil®
Product Description: An extremely potent equine anesthetic used for rapid immobilization of free-ranging and captive members of Cervidae. Formulated as 4-46mg/ml Carfentanyl Citrate, WIL22001, produces rapid immobilization following intramuscular injection.

Section 2 Hazardous Ingredients/Identity Information

Hazardous Component	CAS #	% by Wt	ACGIH TLV	OSHA PEL
Carfentanyl Citrate	61380-25-6	0.45	Unknown	Unknown
Sodium Chloride	7647-14-5	0.80	N/A	N/A
Sterile Water for Injection	7732-18-5	98.55	N/A	N/A

Section 3 Physical/Chemical Characteristics

Appearance: Clear Liquid
Boiling Point: 100 °C
pH: 3.0-4.5

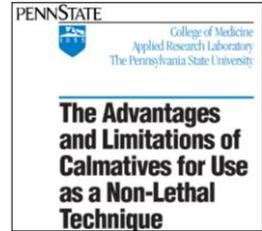
Odor: None
Specific Gravity: 1.023
Vapor Pressure: 23.756 mmHg @ 25°C
Water Solubility: Completely Soluble



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"

(nid2.af.psu.edu/documents/calmativie_report.pdf)



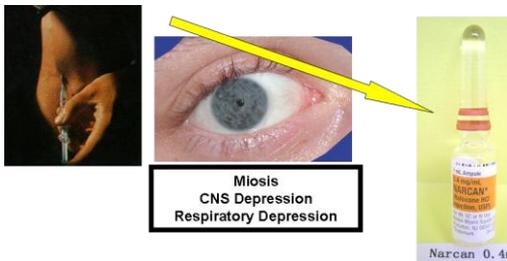
Inhaled Calmatives/Sedatives

- Aerosolized drugs
 - GABAergic agents
 - Benzodiazepine (e.g. diazepam)
 - Barbiturate (e.g. pentobarbital)
 - Opioids
- Volatile agents
 - Hydrocarbons

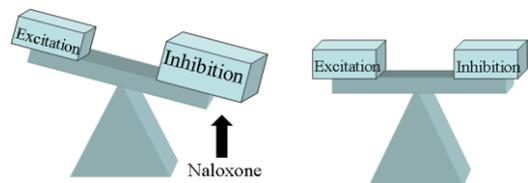
Calmatives/Sedatives

- 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

Rapid Recognition leads to Urgent Intervention



Treatment strategy



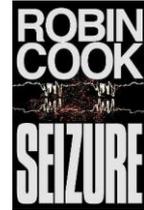
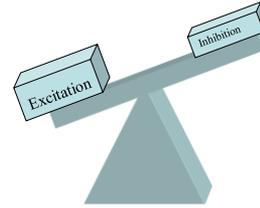


Management of Calmative / Sedative Poisoning

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

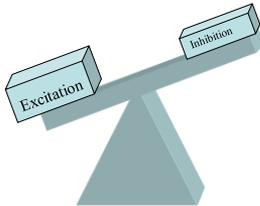


Clinical Syndrome: Convulsions

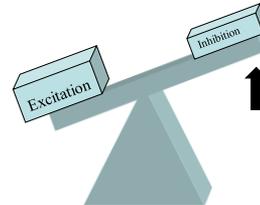


Convulsions

- 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



MMWR 2003;52:159-201

Vol. 52 / No. 10

Poisoning by an Illegally Imported Chinese Rodenticide Containing Tetraethylenedisulfotetramine — New York City, 2002

Illegally imported foreign products can result in domestic exposures to untested 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 tetraethylenedisulfotetramine (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: 80–110 mg/dL). Despite aggressive therapy with lorazepam, phenobarbital, and pyridoxine, the child deteriorated, general tonic-clonic activity for 4 hours and required intubation.

FIGURE: Package of Chinese rodenticide implicated in the poisoning.

Photo: New York City Poison Control Center



THE NEW YORK TIMES INTERNATIONAL WEDNESDAY, SEPTEMBER 18, 2002

Man Admits Poisoning Food in Rival's Shop, Killing 38 in China

By KAREN KROEMER
BEIJING, Sept. 17 — A public health official said today that a man admitted poisoning food in a rival shop in Shanghai in August, resulting in the deaths of 38 people, mostly school children and their parents, in a case that has become known as the "rice ball" poisoning.

The man, who is now in custody, admitted to poisoning the food in a shop in Shanghai in August, resulting in the deaths of 38 people, mostly school children and their parents, in a case that has become known as the "rice ball" poisoning.

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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

www.chinaview.cn 2003-09-29 11:21:01

BEIJING, Sept. 29 (Xinhua) -- 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.



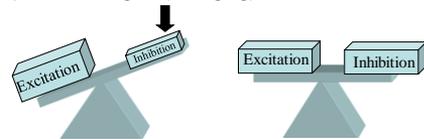
Some Chemical Causes of Convulsions

- 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”



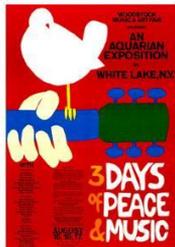
Hallucinogens

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



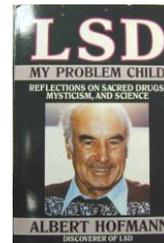
Serotonergic Hallucinogens

- 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



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 Herzegovina.

"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 from the UN Safe Area were unclear - began to hallucinate and behave in an unpredictable way, with some even killing their friends or themselves."

BZ: 3-Quinuclidinyl benzilate (QNB)
Hay A. Surviving the impossible: the long march from Srebrenica. An investigation of the possible use of chemical warfare agents. Med Confl Surviv 1998;14:120-55.



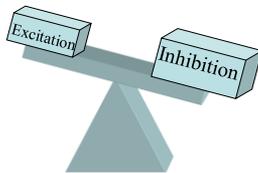
Anticholinergic Hallucinogens

- Qualitatively similar

	Atropine	Scopolamine	BZ
Dose (70 kg)	8-14 mg	2 mg	0.5 mg
Duration	4-8 h	2-4 h	48-72 h



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.



Questions?