

Slide 1

CWMD

## Fourth Generation Agents (FGA)

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Slide 2

### Background and Purpose

- Introduction to Fourth Generation Agents (FGAs)
- Summarize guidance for emergency response community
- Information based on the January 2019 White House National Security Council-led First Responder Working Group effort on FGA information sharing to First Responders and Hospital Communities
  - <https://chemm.nlm.nih.gov/nerveagents/FGAReferenceGuide.htm>
- *There is no credible threat to the United States – this is for educational purposes*

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Slide 3

### What are FGAs?

- A type of organophosphorus nerve agent
- Fourth generation agents (FGA) – aka Novichok, aka A-series agents
  - 1st generation chemical warfare agents (phosgene, chlorine, mustards)
  - 2nd generation: G-series nerve agents (sarin, soman)
  - 3rd generation: V-series nerve agents (VX)
- Developed as weapons by Soviet Union to defeat Western countermeasures
- Recently utilized in a deliberate attack on two individuals in the UK (2018)

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### What are FGAs?

- "A-Series"
  - A-230
  - A-232
  - A-234
- FGAs inhibit acetylcholinesterase, causing cholinergic crisis
- High toxicity/potency, similar to VX
- Unique characteristics pose challenges to response operations



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### FGA Chemical Properties

- Can be persistent in the environment
- Extremely low vapor pressure, 5X lower than VX
- High water solubility but,
- High chemical stability
- Likely to be encountered as a liquid
- Most likely exposure absorbed through skin and mucous membranes (sometimes in significantly delayed fashion) but other routes possible
- Limited data are available from research studies or experiences



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### What Happened in England, March 2018?

- Deliberate attack resulting in two primary exposures and multiple secondary exposures
- Provides incredibly valuable learning points for responders
- There is **NO KNOWN THREAT IN THE US OR INDICATIONS OF POTENTIAL USE IN US**





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### Sergei Skripal


- Former Russian military intelligence officer who acted as a double agent for the UK during the 1990s-2000s
- Arrested by Russian FSB and was convicted of high treason
- In 2010, he settled in the UK following a spy swap
- March 4, 2018 Sergei (66) and daughter Yulia (33) were poisoned with "novichok"



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### Novichok Exposure Timeline



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### First Contact


- EMS finds two individuals altered on a park bench
  - Male-GCS of 13, pinpoint pupils staring into distance, "eyelid movements"
  - Female-GCS of 3, pinpoint pupils
- Intra-nasal naloxone given with "some" response
  - Male received intra-nasal naloxone with some arousal
    - \* Response vs foreign object in the nose?
  - Female without significant response
- Accidental dose of atropine instead of naloxone given
  - Male heart rate goes from 40's to 80's


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### Was It Obvious On Presentation?

- Cholinergic Crisis versus an "Adulterated Opioid"
  - Overt / on-going salivation = No (but drooling – yes)
  - Sweating = Yes
  - Lacrimation= No
  - Urination = No
  - Defecation = No
  - Emesis = ? after naloxone
  - Miosis =Yes
  - Decreased Level of Consciousness = Yes
  - Seizure = No
  - Fasciculations = ? Yes -eyelids
  - Bradycardia = Yes





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### Personal Protection Equipment Used

- The key fact to remember is that responders did not know this was Novichok
- Basic precautions were utilized and no first responder was exposed
- Alerts to first responders to be aware of synthetic opioids had just been issued
- They were called to patients slumped on a park bench

**STANDARD PRECAUTIONS SHOULD ALWAYS BE EMPHASIZED!!!**





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### Emergency Department

- Both patients intubated soon after arrival
  - Rocuronium and ketamine were used
- Lactic Acid were both elevated
  - Male was 5.3 mmol/L
  - Female was 13 mmol/L
- Additional laboratories were notable for bicarbonates of 14 mEq/L and pH's around 7.1-7.2
- Basic supportive care, fluids, and antibiotics started on the male for "aspiration"
- Admitted to a closed ICU service



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12

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### Hospital Course Overnight

- Bradycardia became more prominent with a recorded heart rate of 12 – responsive to atropine
- Significant sweating started to occur such that the nurses were changing the sheets
  - Neither patient was ever febrile
- By 18 hours post exposure (determined retrospectively) there was more of a cholinergic toxidrome
  - Diaphoresis, Bradycardia, Miosis
- Patients became more hemodynamically unstable and started on vasopressors



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13

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### Hospital Course Continued

- Hands were noticed to be disproportionately blue
- Now at 24-30 hours patients becoming more ill
  - Simultaneously, police inform hospital staff to “google” patient
  - A police officer involved on scene presents for a “cloudy” feeling in his head
  - Notable lab findings from the male/female now show a Na 157 mEq/L and K 2.5 mEq/L
    - \* RTA from poisoning vs vomiting vs other were considered



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14

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### Hospital Course Continued

- ICU physicians sign out to a new team
  - Noting this is not consistent with an opioid
  - Considered a “pesticide” but after reading more did not pursue testing due to no pulmonary edema, or respiratory symptoms at all
- Given the background of the patient and past events radiation was evaluated and ruled out
- Multiple consultants were brought into the picture and cholinesterase testing and identification occurred



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15

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### Clinical Course

- Throughout the hospital course, anticholinergics and pralidoxime were initiated:
  - Anticholinergics
    - Scopolamine 400 mcg SQ Q8hours
    - Atropine 2 mg bolus followed by infusion titrated to heart rate 60-70
  - Oximes
    - Pralidoxime 30 mg/Kg bolus followed by 8 mg/Kg/hr

**Clinical Observation:** Pralidoxime improved hemodynamic stability and urine output. When weaned early, urine output dropped and hemodynamics worsened. Parameters improved when pralidoxime was restarted



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### Secondary Exposures During Investigation

- One police officer presumably exposed by improperly removing glove (touched exposed outside surface of glove) → Hospitalized, not critical
- One police officer exposed → Not hospitalized, miosis only



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### Secondary Exposures : Months Later

- Two individuals discover perfume bottle in trash
- Patient one dies
- Patient two – critically ill





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### Remediation

- Significant challenges in communications with the public (instructions on what public should do)
- Challenges with those concerned about exposure
- 12 sites secured and cleared (up to one year to complete all)
  - 13,000 man-hours spent in protective gear
  - 5,000 samples processed



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### First Responder Considerations

- Cutaneous exposure can result in significant delays in symptom development
- Could result in multiple areas of contamination
- A real probability that FGA poisoning would not be recognized initially
  - Universal Precautions
- Clues
  - Atypical "found down" scenarios – very difficult

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Slide 21

### First Responder Considerations

- FGAs are highly potent; contacting small amounts can cause serious toxicity
- Responders must take measures to prevent direct contact with:
  - Liquid agent (dermal or eye contact with liquid most likely route)
  - Suspected contaminated surfaces
  - Potentially contaminated people
- Detection
  - Most capabilities to detect FGAs resides with specialized resources in the USG (WMD-CSTs and FBI WMD)
  - M-8 paper may produce a unique color reaction
  - DoD and DHS are examining broader share of FGA spectral libraries with detector manufacturers

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First Responder Considerations: Protection

- Adherence to basic PPE (gloves including proper donning of gloves)
- Decontaminate with soap and water
  - RSDL can be used for spot decontamination if available
  - Avoid bleach: Skin irritation in the setting of likely dermal exposure and reports of combustion with RSDL
- Secure vehicles, facilities, and items that may have been exposed
- Considerations for follow up on staff

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22

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First Responder Considerations

- Technical assistance
  - Identification
    - \* Contact FBI WMD Coordinator
    - \* National Guard WMD-CST
  - General background information
    - \* CHEMM website
    - \* ASPR TRACIE website: linked to USG interagency group of SMEs
  - Exposure and healthcare related topics
    - \* Poison Control Centers

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23

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Slide 24

Hospital Considerations

- First responder lessons apply
- There is the real probability that FGA poisoning would not be recognized initially
  - Symptoms evolved over the course of the first 24 hours
  - Some initial symptoms appeared consistent with narcotic overdose
- Clues:
  - Persistent bradycardia despite addressing respiratory depression
  - Persistent respiratory depression despite adequate narcotic antidote
  - Profound metabolic acidosis
  - Emerging cholinergic crisis symptoms (sweating without fever)

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24

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Slide 25

### Hospital Considerations: Protection

- Must re-emphasize universal precautions
  - Due to low vapor pressure, off-gassing less likely
- There is some evidence that double gloving and changing gloves every 15 minutes can increase protection for repeated patient contact
- Healthcare providers NOT LIKELY to wear Level A or B PPE so patient decontamination is important



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25

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Slide 26

### Hospital Considerations: Decontamination

- Decontaminate with soap and water
  - FGAs are not hydrolyzed by water – contain run off if possible
- Delayed decontamination or repeat decontamination is likely beneficial based on Salisbury
- RSDL can be used for spot decontamination if available



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26

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Slide 27

### Hospital Considerations: Treatment

- Use existing nerve agent treatment protocols
  - Atropine, pralidoxime, benzodiazepines for seizures
- May require higher doses and longer duration of treatment
- Medical countermeasure shortage may be an issue
  - Chempack utilization
  - Contingency Medical Countermeasures



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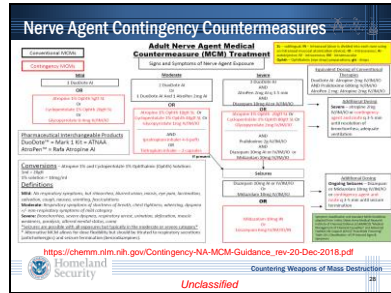
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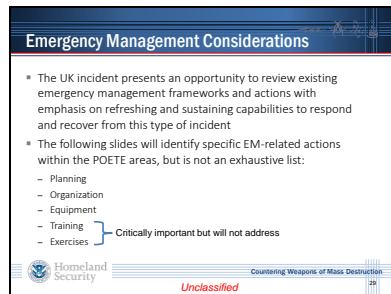
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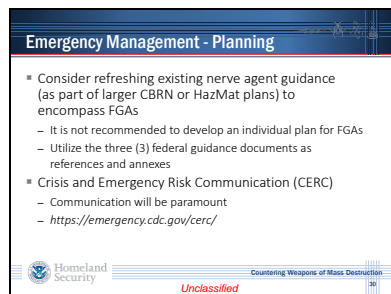
Slide 28



Slide 29





Slide 30



Slide 31

### Emergency Management - Organization

- Ensure that organizational relationships exist between stakeholders that would be involved in response and recovery, particularly state and federal agencies
  - Review your multi-agency coordination and ICS frameworks
  - Know where to get accurate technical information on FGAs:
    - \* FBI Weapons of Mass Destruction (WMD) Coordinator
    - \* National Guard WMD-CST
    - \* Poison Control Center
    - \* CHEMM and WISER websites / tools
    - \* ASPR TRACIE website



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Slide 32

### Emergency Management - Equipment

- Please refer to the 3 White House released documents for specific equipment/ resources
- Remember your state/federal partners that could augment local supplies
- Scene remediation will be extensive



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Slide 33

### Conclusions

- Developed FGA guidance is protective based on current information available
- Efforts to limit spread is important due to extreme difficulties in detection highlighting explicit use of standard precautions and protocols
- Federal resources on FGAs exist and pre-planning will lead to optimizing the response



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