SANITÄTSDIENST

# DIFFERENTIATING NERVE AGENT POISONING FROM OPIOID POISONING – CLINICAL SIGNS, DETECTION AND DIAGNOSTICS

PD Dr. Timo Wille LtCol (MC) German Armed Forces
Bundeswehr Institute of Pharmacology and Toxicology

BUNDESWEHR

# Disclosures

Presenter's  has no relevant financial or non-financial interests to disclose.

Disclosure will be made when a product is discussed for an unapproved use.

This continuing education activity is managed and accredited by AffinityCE in collaboration with AMSUS. AffinityCE and AMSUS staff as well as Planners and Reviewers, have no relevant financial or non-financial interests to disclose.

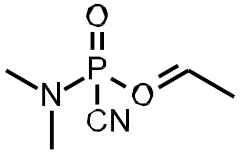
Commercial Support was not received for this activity

# Objectives

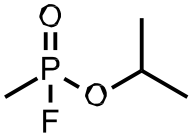
- List clinical signs of nerve agent and opioid poisoning
- Know that highly potent opioids might be misused as chemical weapon
- Know on-site devices for diagnosis of opioid and nerve agent poisoning

# NERVE AGENTS – RELEVANCE

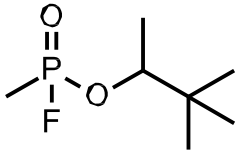
Salisbury / Amesbury 2018: one death, min. four injured
Kuala Lumpur 2017: one death
Syria 2013-2017: thousands dead and injured
Halabja 1988: 5.000 deaths, 10.000 injured



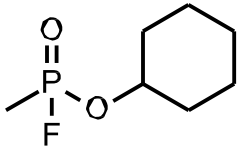

**Tabun (GA)**



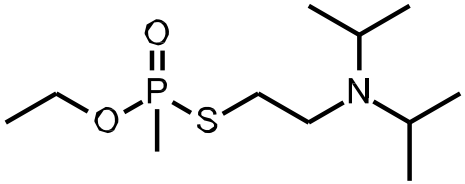

**Sarin (GB)**




**Soman (GD)**




**Cyclosarin (GF)**

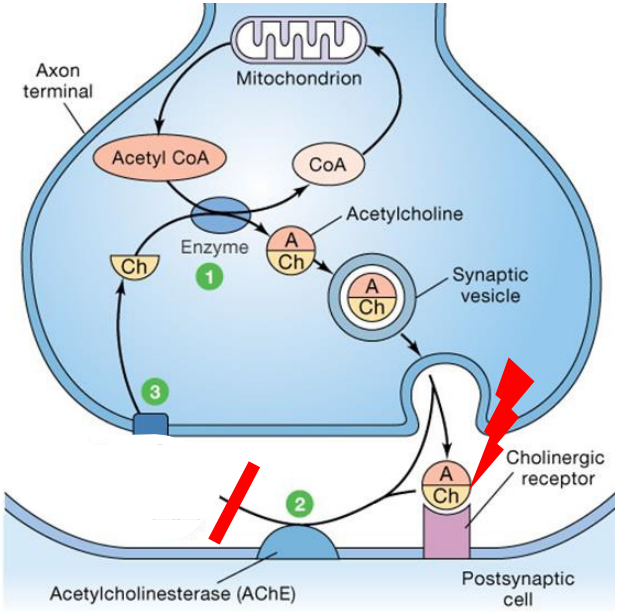



**VX**

Novichok?

# MECHANISM OF NERVE AGENT POISONING – INHIBITION OF ACETYLCHOLINESTERASE

**Physiology:**
Acetylcholinesterase (**AChE**) **cleaves acetylcholine** in acetate and choline and **terminates** its action as a **neurotransmitter**



faculty.pasadena.edu

**Pathophysiology:**
**Binding of OP** to AChE, renders the **enzyme inactive**
→ **ACh overflow** at muscarinic and nicotinic synapses

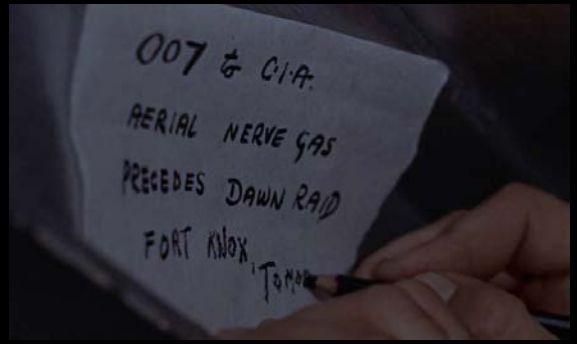
| **muscarinic** | **nicotinic** | **cns** |
|---|---|---|
| diarrhea | muscle fasciculations | seizures |
| bradycardia | cramps | |
| bronchorrhea, bronchoconstriction | severe muscle dysfunction | respiratory disturbance |


londonlungcancer.com


aic.cuhk.edu.hk/Muscle


dailymail.co.uk

# Fleming‘s Goldfinger (novel 1959 / movie 1964)





- Goldfinger advocates “a highly concentrated opiate….the symptoms are a deep and instant sleep” to enable a raid on Fort Knox
- 1960: discovery of fentanyl by Janssen

Images: bondmovies.com; goldfinger.neocities.org

Sanitäts dienst

# OPIOIDS = NEW CHEMICAL THREAT

## Moscow Theater Siege 2002

Terrorists take > 800 hostages

aerosol pumped by SOF:

33 dead terrorists

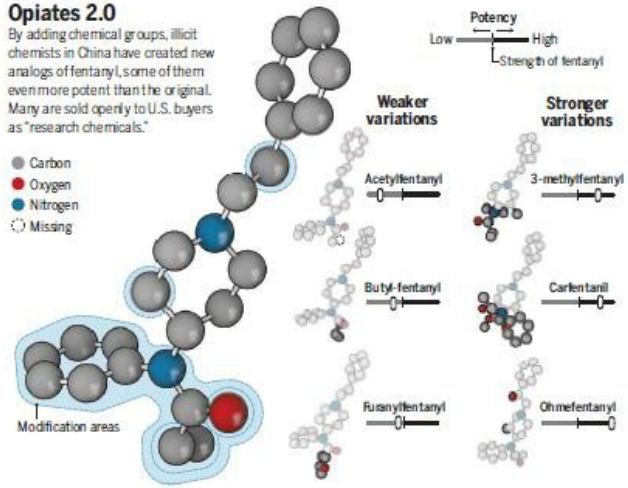
125 dead hostages

**Analysis of Clothing and Urine from Moscow Theatre Siege Casualties Reveals Carfentanil and Remifentanil Use**

James R. Riches, Robert W. Read, Robin M. Black, Nicholas J. Cooper and Christopher M. Timperley*

Detection Department, Defence Science and Technology Laboratory (Dstl), Porton Down, Salisbury, Wiltshire, SP4 0JQ, UK

## Fentanyls




Two milligrams of fentanyl—just a few grains clinging to a sample vial—is a lethal dose.

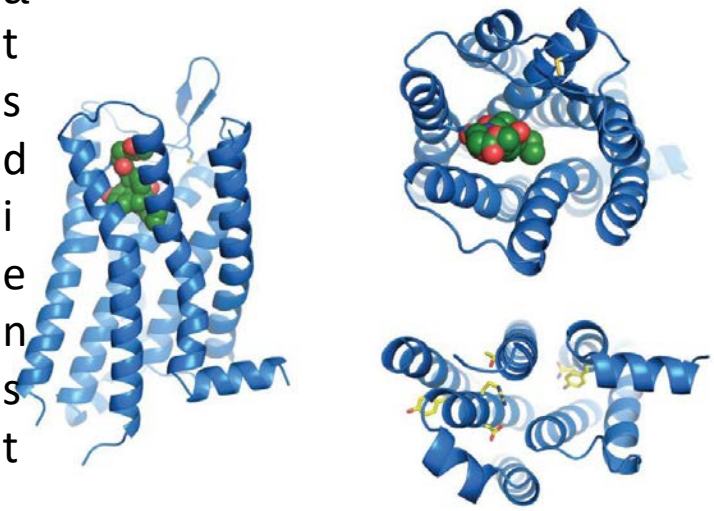
Deadly doses

Fentanyl = 2 mg

(VX = 4 mg)

# MECHANISM OF OPIOID POISONING – INHIBITORY GPCR

Therapy:
μ-agonism results in analgesia



Opioid toxidrome:
Miosis, CNS depression, respiratory depression,

wikimedia.org

dailymail.co.uk

| delta | kappa | mu |
|---|---|---|
| analgesia | analgesia, miosis, sedation | analgesia, miosis, respiratory disturbance |

# SIMILAR CLINICAL SIGNS FOR OPIOIDS AND NERVE AGENTS

„When you hear hooves: Think Horses not Zebras“

Covered bench near shopping center in Salisbury where collapsed victims were found

tentative diagnosis: opioid poisoning

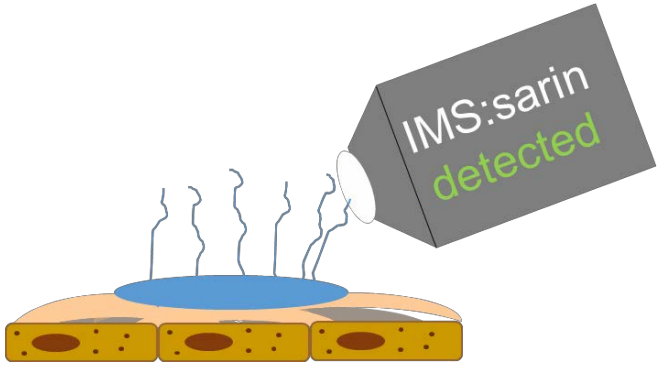
| | Initial Toxidromes in Order of Onset → Continuous; depends on route of uptake and dose | | | |
|---|---|---|---|---|
| Class | Primary | Secondary | Tertiary | Later Signs |
| Nerve agents | mental-status changes, fasciculations, muscle weakness, paralysis | increased secretions, miosis | shallow breaths | convulsions, coma, respiratory arrest |
| Opioids | confusion, miosis | bradypnea, sedation, apnea | coma | respiratory arrest, bradycardia, hypotension |

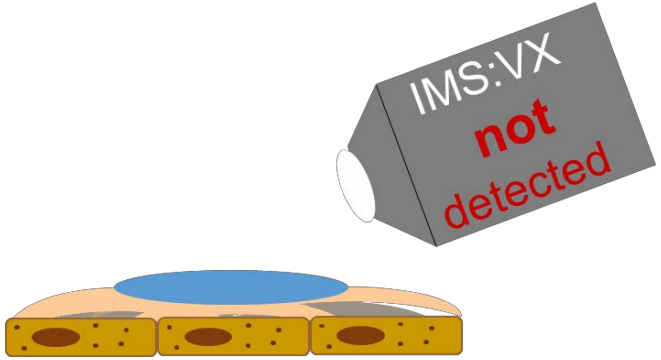
# ASSUMPTIONS – OPIOID VS NERVE AGENT POISONING

- Toxidrome-based triage might fail in discrimination of opioids and nerve agents
- Nerve agents and opioids are lethal if not quickly diagnosed
- Nerve agents and opioids require different antidotes

Need for discrimination of both groups → early detection and identification on surfaces and/or skin

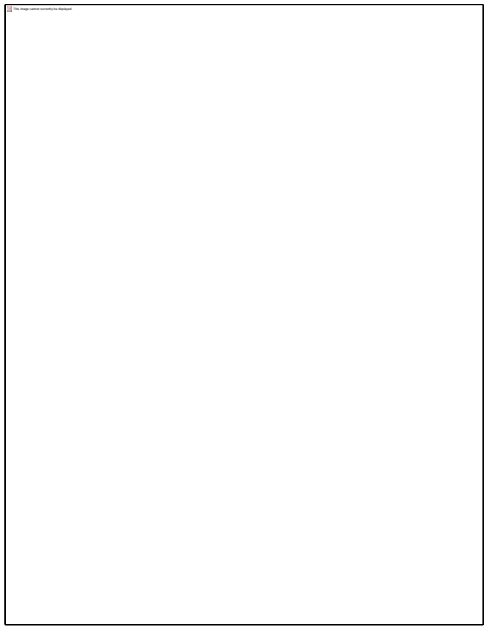
# SKIN DETECTION - KEY ASSET IN MANAGEMENT OF CHEMICAL MASS CASU



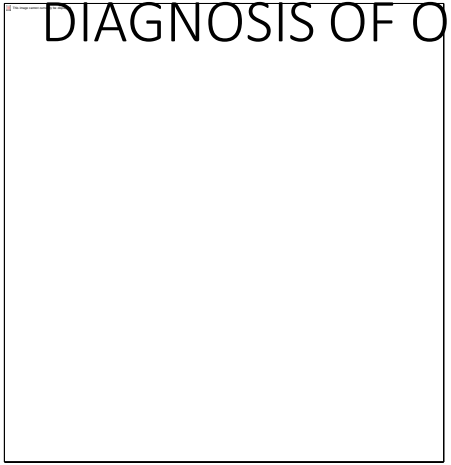

Gap: detection of nerve agents with low vapor pressure and high percutaneous toxicity such as V-agents

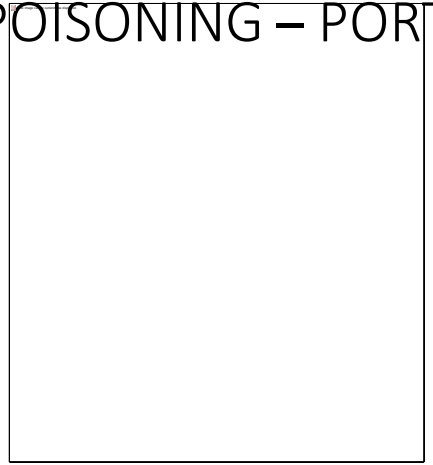
Kit covers **all** AChE inhibitors!



OP Skin Disclosure Kit is in advanced development !

# DIAGNOSIS OF OP POISONING – PORTABLE DEVICE FOR FIELD USE





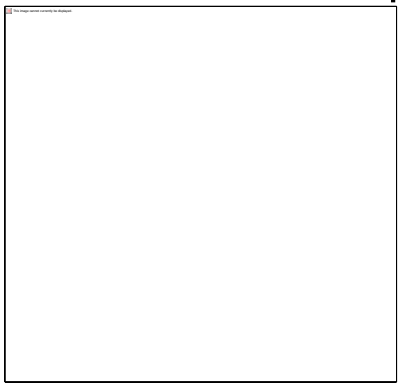
Development of medical product:

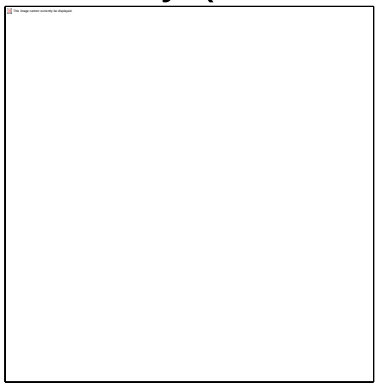
ChE check mobile: covers all AChE inhibitors, easy to use, robust, field-usable, COTS

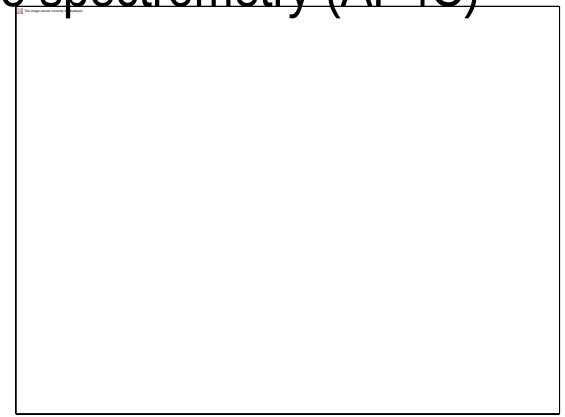
Nerve agent poisoning: Yes or No

# FENTANYLS – ON SITE DEVICES

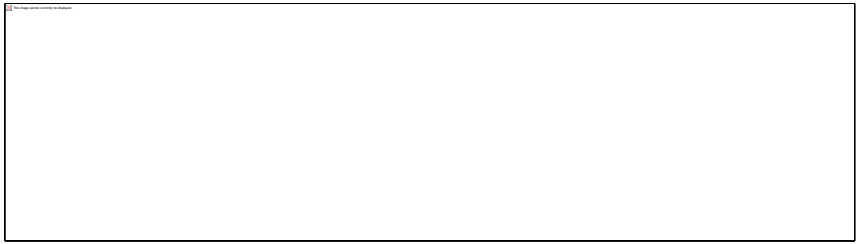
Detection: Mass Spectrometry (MS; MX908), flame spectrometry (AP4C)







Diagnosis (ELISA for saliva, sweat, urine; spectrum?)



# CONCLUSION

- Highly potent opioids (fentanyls) might be mis-used as chemical weapons
- →synthesis of fentanyls is comparable easy (convenient one pot synthesis of fentanyl)

- Toxicity of fentanyls is comparable to toxicity of nerve agents – both lethal if not treated quickly
- →both groups pose risk for first responders

- Opioids and nerve agents might show similar signs - but differ largely in antidotal treatment
- → tool for skin detection of nerve agents is under advanced development
- → tool for diagnosis of nerve agent exposure is available
- → tools for detection and diagnosis of fentanyls available (spectrum?)
- → supportive care may ultimately be life-saving (ventilation)

# CONTINUING EDUCATION

- How to Earn CE If you would like to earn continuing education credit for this activity, please visit: http://amsus.cds.pesgce.com
- Hurry, CE Certificates will only be available for 30 Days after this event!

# DIFFERENTIATING NERVE AGENT POISONING FROM OPIOID POISONING – CLINICAL SIGNS, DETECTION AND DIAGNOSTICS

Thank you for your attention!

Questions?