

SELF ASSESSMENT EXERCISES

Self Assessment Exercises In Toxicology

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A General Duties Medical Officer may be involved in a spectrum of toxicological emergencies from an adverse drug reaction (ADR) to a chemical warfare (CW) attack. Knowledge of the threat is essential, as well as identifying and managing the effects of a specific agent. Differentiating the type of incident may be difficult. The use of antidotes depends on the status of the casualties, and it should be remembered that antidotes have their own side effects.

For the purpose of the following series of questions, you are a GDMO deployed to a Field Hospital during Peace Support Operations in a post-conflict industrialised country. Despite Host Nation Support, there remains a significant asymmetric/terrorist threat with a credible CW capability. Personnel are therefore carrying respirators and combopens.

1. A patrol encounters a number of drums in what appears to be a deserted farm. One soldier comes into contact with liquid and vapour from a leaking drum. Within minutes, he is complaining of dimmed vision, chest tightness and breathing difficulty. Other members of the patrol come to his aid and removed him from the scene. They also experience mild symptoms.

- What is the liquid likely to be and is it a chemical warfare agent?
- What is the initial priority of the other members of the patrol?
- Which toxidrome* best describes the syndrome experienced by the casualty?
- What antidotes may be appropriate for this type of poisoning?

2. During the preparation phase, the pre-deployment brief highlighted a significant terrorist threat that included the use of chemical agents. Part of the initial management of contaminated casualties is decontamination.

- Place the following agents in order of persistency, from least to most (mustard, hydrogen cyanide, sarin).
- What is the term used when rescuers are also affected by chemical agents after the initial exposure has passed?
- What common household agent is used to assist decontamination, and at which

concentrations?

- Can you initiate medical treatment before a casualty has been decontaminated?

3. You receive a report of an incident within a building, where an agent, thought to be a gas, has been released. There is rapid onset of symptoms among those affected including disorientation, dyspnoea, and loss of consciousness. Some casualties are fitting and there are reports of fatalities. After removing casualties from the building emergency responders notice that some casualties appear pink while others appear cyanosed. The agent is non-persistent and some of the mild cases recover spontaneously. The more severe cases are assessed and resuscitated, and when intravenous access is gained in many cases the blood appears bright red.

- What is the likely agent?
- What is the mechanism of toxicity and why may some casualties appear pink with bright red venous blood?
- What antidotes may be used in these cases?

4. During the same incident a casualty arrives at the Field Hospital, and it is noted that he is markedly cyanosed. One of the medical assistants comments that he looks as "blue as a smurf". Initial observations reveal a pulse rate of 120 beats per minute, blood pressure 95/60, respiratory rate 40 breaths per minute, with unrecordable oxygen saturations. While taking blood, the medical assistant notes that the blood looks brown.

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* A toxidrome is a term used to describe a specific syndrome due to a pharmacologically active agent (toxin).

- a. What is the diagnosis?
 - b. What agent is the cause?
 - c. What recreational drug may cause the same condition?
5. Following the incident, several personnel require medical attention for their injuries. Some of them have administered their own CW medical countermeasures. One casualty was found wandering around outside the scene of the incident in a confused state. Examination reveals a pulse rate of 130 beats per minute, blood pressure 110/80, respiratory rate 25 breaths per minute, oxygen saturations 98%, with dilated pupils and dry mucous membranes.
- a. What is the toxidrome?
 - b. What is the likely cause?
 - c. What other observation should be noted and why should physical restraint be avoided in these cases?
6. A couple of days later a member of the field hospital staff is found unconscious within the compound. He smells of alcohol but there are no bottles or other clues to suggest a cause for his state. On arrival in the Emergency Department his pulse rate is 100 beats per minute, blood pressure 110/60, respiratory rate 6 breaths per minute, oxygen saturations 90% on air, and he has pinpoint pupils. He responds to painful stimuli. His BM is 6, and there is no external evidence of injury.
- a. What is the likely diagnosis?
 - b. What is the specific antidote for this type of poisoning?
 - c. What other condition should you include in your differential diagnosis?
 - d. What other drug may be implicated?
 - e. How would the lack of an assay for this drug affect the management of the case?

Answers to self assessment questions

Question 1

- a. Organophosphate pesticide. No, although nerve agents are organophosphates.
- b. Safety should be their priority.
- c. Cholinergic.
- d. Atropine, oxime (pralidoxime) ± a benzodiazepine.

Table 1. Cholinergic Symptoms (predominant symptoms in bold) (1).

Muscarinic symptoms	Nicotinic symptoms	Central symptoms
Miosis	Mydriasis	Agitation
Bradycardia	Tachycardia	Confusion
Bronchorrhea, bronchospasm	Bronchodilation	Lethargy
Vomiting, diarrhoea	Hypertension	Coma
Salivation, lacrimation	Diaphoresis	Seizure
Urinary incontinence	Weakness	Death



Discussion

Organophosphate pesticides are still widely used throughout the world, and occasional cases still occur in the UK, usually due to exposure to sheep-dip. Organophosphates are also the class of agent used in the manufacture of nerve agents. The toxicity of organophosphates (and nerve agents) is due to an irreversible binding of the agent to the enzyme cholinesterase. This enzyme breaks down the neurotransmitter acetylcholine and allows the nerve to repolarise. Inhibition of this enzyme results in the accumulation of acetylcholine at receptor sites and overstimulation. Acetylcholine is found within the brain, at preganglionic synapses of the sympathetic and parasympathetic system (nicotinic), at the postganglionic parasympathetic neurons (muscarinic) and at the neuromuscular junction (nicotinic). Toxicity results in a cholinergic toxidrome, which is summarised in Table 1.

The treatment of both accidental pesticide exposure and nerve agent exposure, following an assessment of airway, breathing and circulation, should include administration of atropine to reduce secretions and assist breathing. Pralidoxime (an oxime), if given early, reduces the affinity of the binding site on the cholinesterase to the organophosphate, and may reduce the total atropine required as well as reducing nicotinic effects. However, oximes do not antagonise any of

the central effects. Benzodiazepines may be required to control seizures. All three agents are present in combopens (2).

As with any incident site, the priority of any first responder is personal safety. This is particularly important in cases of a chemical release where there may be no obvious signs and there is the potential for contamination as well as direct intoxication.

Knowledge of different toxidromes can be applied to the initial assessment of chemical casualties using a system similar to the primary survey used by the Advanced Trauma Life Support (ATLS) guidelines (see Figure 1).



AIRWAY

SECRETIONS	Increased?	→	NERVE AGENT
	Decreased?		ATROPINE / BZ
ODOUR	Bad Eggs?	→	SULPHIDE

BREATHING

BREATHING	Bronchospasm?	→	NERVE AGENT
	Cough and frothy sputum?		LUNG DAMAGER
SKIN COLOUR	Cyanosis?	→	CYANIDE METHAEMOGLOBINAEMIA
	Pink?		CYANIDE CARBON MONOXIDE

CIRCULATION

HEART RATE	Bradycardia?	→	NERVE AGENT
VENOUS BLOOD	Chocolate coloured blood?	→	METHAEMOGLOBINAEMIA
	Arterialised venous blood?		CYANIDE

DISABILITY

PUPILS	Pinpoint?	→	NERVE AGENT	OPIATE
	Dilated?		BOTULIN TOXIN	ATROPINE / BZ
CNS INVOLVEMENT – Confusion, Coma		→	NERVE AGENT	ATROPINE / BZ

EXPOSURE

ERYTHEMA/ BURNS	Immediate (<1 hr)?	→	HYDROFLUORIC ACID	LEWISITE
	Delayed (>1 hr)?		MUSTARD	
MUSCLE	Fasciculation?	→	NERVE AGENT	
	Flaccid paralysis?		BOTULIN TOXIN	
SKIN	Excessive sweating?	→	NERVE AGENT	
	Dry?		ATROPINE / BZ	
NEAR PATIENT TESTING	↑ Lactate? ↓ Bicarbonate?	→	CYANIDE	

Fig 1. Chemical Primary Survey.

Question 2

- Hydrogen cyanide (least persistent), sarin and mustard (most persistent).
- Secondary contamination.
- Bleach (sodium hypochlorite), 0.5% is used for casualty decontamination (5% may be used for equipment).
- Yes – emergency life saving treatment is still possible.

Discussion

Secondary contamination is when rescuers are affected by chemicals present on casualties, rather than from the primary incident site (known as the dirty or hot zone). The greatest hazard is from persistent agents that may be liquid or thickened non-persistent agents. Gases (with low boiling points) will be the least persistent, followed by liquids with higher vapour pressures. Persistency also depends on ambient conditions such as wind, ground and air temperature.

For contaminated casualties, the decontaminant of choice is 0.5% hypochlorite solution, which removes, hydrolyses and neutralises most chemicals. It should not be used around the eyes, mucous membranes or open wounds. Equipment including the respirator should also be decontaminated and returned to the casualty.

Although decontamination is a priority, emergency medical management should not be delayed if a casualty is contaminated. This is especially true for combined injuries (conventional and chemical intoxication). Triage of casualties still applies and includes prioritisation of airway, breathing and circulatory problems. Many guidelines advocate concurrent decontamination and emergency medical interventions. Current military doctrine advises early use of combopens before decontamination (3,4,5).

Question 3

- Cyanide (as hydrogen cyanide).
- Arterialisation of venous blood due to inhibition of intracellular respiration.
- Sodium (or amyl) nitrite followed by sodium thiosulphate or Dicobalt edetate or Hydrocobalamin (vitamin B12a).

Discussion

Cyanide poisoning causes an inhibition of intracellular respiration. This is due to the binding of cyanide to the ferric ion of mitochondrial cytochrome $a-a_3$ causing a lactic acidosis due to anaerobic respiration. Cyanide toxicity is characterised by its rapid

onset and symptoms include headache, confusion, dizziness, dyspnoea, cardiovascular collapse and coma. Seizures may also occur.

Signs are generally non-specific but the casualty may initially appear pink, then cyanosed. Arterialisation of venous blood is due to a high oxygen tension and saturation of haemoglobin due to the lack of oxygen use and extraction by the tissues. A venous sample showing a high lactate, high partial pressure of oxygen and acidosis may assist the diagnosis.

Treatment should include high flow oxygen. Antidotes exploit the high affinity of cyanide for certain compounds that include ferric, cobalt and sulphur groups. The most widely used antidote uses two agents, a nitrite (sodium or amyl) and sodium thiosulphate. Nitrites cause methemoglobinemia, and cyanide is drawn back into the intravascular space. Thiosulphate binds to cyanide, forming the less harmful thiocyanate, which is then eliminated by the kidneys. Dicobalt edetate and hydrocobalamin (vitamin B12a) are both cobalt compounds that bind directly to cyanide. All cyanide antidotes should be used with caution due to potential side effects, especially in the absence of cyanide (6).

Question 4

- Methemoglobinemia (MetHb).
- Sodium nitrite.
- Amyl nitrite (poppers).

Discussion

A number of agents can cause methemoglobinemia. In this case, it is likely to be due to sodium nitrite, used as an antidote to cyanide. Other causes include a congenital metabolic insufficiency, and other drugs such as prilocaine, nitrites and nitrates. Nitrites are sometimes used recreationally and are known as “poppers”. Some industrial chemicals, including aniline, dyes, may also cause this condition.

Symptoms are due to a decrease in the oxygen binding capacity of haemoglobin, similar to the effects of carbon monoxide poisoning. Anaemia can cause more severe symptoms due to a higher percentage of iron being converted from the ferrous (Fe^{2+}) to ferric (Fe^{3+}) state, an important consideration if there has been trauma and blood loss. Another contraindication for the use of nitrites in cyanide poisoning is smoke inhalation due to the combined effects with carbon monoxide on haemoglobin. Treatment of methemoglobinemia should include high flow oxygen, and methylene blue is a specific antidote (7,8,9).

It is important to remember that many antidotes have significant side effects and

treatment should be based on a risk assessment. This assessment should take into account the effects of the toxic chemical and the potential side effects of the antidote.

Question 5

- Anticholinergic (antimuscarinic) syndrome.
- Atropine (inappropriate self-administration of a combopen).
- Core temperature. Physical restraint may precipitate drug-induced hyperthermia due to loss of peripheral vasodilatation and sweating.

Discussion

Accidental or inappropriate use of a combopen may lead to toxic side effects of the anticholinergic agent atropine. This centrally acting drug may cause symptoms and signs including dilated pupils, blurred vision, confusion, dry skin and mucous membranes and tachycardia. Some incapacitating agents such as BZ are potent long acting anticholinergics. It is important that other causes of these symptoms and signs such as trauma, psychological stress and delirium are excluded. Treatment is generally supportive although the antidote physostigmine is sometimes necessary.

Because of the reduction in sweating, drug induced hyperthermia should be actively excluded, and as physical restraint may precipitate this, it should be avoided (2).

Anticholinergics are widely used in a variety of preparations. Atropine is used in Advanced Life Support protocols for the treatment of bradycardia and asystole. Ipratropium (atrovent) is used as a bronchodilator, either in powdered or nebulised form. The group of drugs originates from plants such as the deadly nightshade (*Atropa belladonna*).

Question 6

- Opiate poisoning, possible analgesic overdose.
- Naloxone.
- Pontine stroke.
- Paracetamol.
- In cases where a significant paracetamol overdose (>12g or 150mg/kg) is possible and a level will not be available within 8 hours antidote treatment (N-acetylcysteine) should be started.

Discussion

The most common presentation of chemical or drug toxicity is analgesic overdose. The most common drug of overdose is paracetamol, but this may be taken in the

form of preparations containing opiates. In this scenario, the immediate priorities remain assessment and treatment of airway, breathing and circulation. The opiate toxidrome classically produces a reduced respiratory drive, reduced conscious level and pinpoint pupils. Dextropropoxyphene (coproxamol) has significant cardiovascular effects even at relatively low doses. The antidote for opiate overdose is naloxone, which is relatively safe but has a short half life (10).

A pontine infarct, or haemorrhage, may also present with impaired consciousness and pinpoint pupils. Local effects on the respiratory centre in the brainstem can cause respiratory depression, giving a clinical picture similar to opiate overdose.

When managing any overdose, paracetamol poisoning should be considered. The effects of paracetamol toxicity appear late and patients may be asymptomatic until after the opportunity for antidote treatment has passed. Simple analgesics are used widely in the operational theatre but with limited biochemistry support. Ideally a paracetamol level should be taken at 4 hours post ingestion, but where levels are unavailable, or will not be available before 8 hours, treatment should be started in significant overdoses. Significant overdoses are defined as >12g (24 x 500mg tablets) or 150mg/kg in the absence of high risk factors. The antidote is N-acetylcysteine, which is a glutathione donor. Glutathione neutralises toxic metabolites and prevents liver damage, the main effect of paracetamol toxicity. N-acetyl cysteine is a relatively safe drug but may cause anaphylactoid reactions (11).

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