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INVITED REVIEW

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Current Risks of Chemical Warfare and Medical Perspective

Kimyasal Savaşın Güncel Tehditleri ve Tıbbi Bakış Açısı

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Abstract

The increasing prevalence of Chemical, Biological, Radiological, and Nuclear (CBRN) threats presents a significant global security concern, particularly in regions which are under conflict and terrorism. This review evaluates the risks associated with chemical warfare agents (CWAs), their pathophysiology, clinical effects, and medical management strategies. It highlights the historical context of CWAs, their mechanisms of toxicity—including nerve, blister, blood, and choking agents—and the severe physiological consequences they impose. More focus is placed on medical preparedness, including early detection systems, protective measures, decontamination protocols, and antidotal therapies essential for mitigating CBRN-related casualties. The role of healthcare professionals is underscored, particularly in rapid triage, treatment strategies, and the necessity of international collaboration in enhancing CBRN defense mechanisms. It is highly recommended that strengthening medical CBRN defense through improved health monitoring, early detection, protective measures, emergency response, and global collaboration is crucial for mitigating the growing threat of CBRN attacks.

Keywords: CBRN threats; Chemical warfare agents; Decontamination; Emergency Medicine; Emergency preparedness; Health care managment; Medical response; Public Health; Terrorism

CBRN (Chemical, Biological, Radiological, and Nuclear) threat is currently is one of the serious security concerns globally. The offensive use of CBRN weapons has shown a rapid increase especially over the last two decades starting from the attacks of September 11, 2001, commonly known as 9/11. Factors such as the availability of agents' sources, the development of systems to deploy CBRN agents in various fields, the ability to produce these agents, having plans and procedures to deploy them, taking necessary protective measures for the country itself, and the use of these weapons in line with national interests demonstrate a country's CBRN weapon capabilities. In the coming period, risks and threats originating particularly from the Middle East are expected to continue affecting regional security, especially for Türkiye. Currently, CBRN weapons are being produced, developed, and stockpiled not only by many developed countries but also by countries governed by totalitarian regimes and those supporting terrorism, as a show of power and superiority against other countries, to balance weaknesses in conventional weapons.[1] Among the potential targets of CBRN weapons are various areas such as governmental offices, military institutions, airports,

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shopping malls, schools, and water delivery facilities.[2,3] Additionally, the use of weapons of mass destruction and harmful substances in ongoing or potential regional wars, their use by terrorist groups, accidents during transportation and smuggling, and the potential for regional disaster effects due to release and leak in nearby nuclear and chemical energy and industrial facilities and research laboratories are potential risk factors.[4]

The aim of this review is to assess the risks, pathophysiology, clinical effects, and medical management of chemical warfare agents under the concept of CBRN threats, focusing on detection, decontamination, and countermeasures. It also aims to enhance awareness among healthcare professionals and policymakers for effective response to CBRN incidents.

The selection of articles for this review was conducted through a systematic search using relevant keywords related to CBRN, chemical warfare agents, threats, terrorism, and medical countermeasures. The time period for the search focused primarily on the last two decades, reflecting the increasing concerns surrounding CBRN threats since the 9/11 attacks. However, historical sources were also included to provide context on the evolution of chemical and biological warfare. The methodology ensured a balanced review of past incidents, current risks, and future preparedness strategies, particularly with a focus on regional threats, including those originating from the Middle East.

An Overview on CBRN Threat

The CBRN threat also brings the risks of the use of weapons of mass destruction and hazardous materials in regional wars and by terrorist groups, its release due to accidents, and nuclear plant accidents. Of those agents, chemical warfare or chemoterrorism agent or weapons also constitute an important part of the CBRN threat. Thus, it is necessary for governments and public to take measures against the CBRN threat and to develop an effective strategy on this issue and to act in international cooperation. Including the management at the incident site, the measures to be taken against this threat will be an important step in ensuring general security and regional stability.[5,6]

The production of chemical warfare agents (CWAs) in the inventories of some developed countries does not require advanced technology and financial resources, and despite all international prohibitions, there is no real barrier to their use. On the other hand, defensive measures which are highly costly require scientific and technological accumulation, and necessitate training and organization, which has ensured the continued relevance of these agents. Due to the possibility of using chemical weapons (CWs) in future conflicts or wars, it has become a necessity for healthcare personnel to be knowledgeable about these agents, their effects, and the treatment of exposed casualties. The purpose of this article is to provide general information about chemical warfare agents and to raise awareness among healthcare personnel on this subject.

CWAs are toxic agents used in military and terrorist activities to kill, severely injure, incapacitate, or render ineffective living masses due to their physiological and biological effects. These weapons also have indirect effects such as contaminating plant and animal food stocks, rendering them unusable, forcing the use of protective clothing and equipment for safety, thereby reducing mobility, and diverting troops in a military operation to undesirable directions. CWs are used not only to kill or incapacitate living beings but also to render economically significant targets inoperable and to create fear and chaos in society.

Chemical warfare is the asymmetric type of warfare conducted using chemical agents in solid, liquid, gas, and aerosol forms, which are made lethal, injurious, and irritating with the help of weapons. CWAs can manifest their effects with all weapons such as cannon, missile, mine, etc. By spraying from a truck or an airplane, it can be mounted on the tip of an arrow or a rocket and used. CWs can also be used by mixing them with air conditioning and ventilation systems or by spraying them into the environment with smoke generators. The production of these agents is easy and cheap, while their poisoning capacities are high. Additionally, their storage, transportation, and inspection are easily facilitated. CWAs can be made more persistent in the environment by using carrier particles such as talc powder or diatomaceous earth. These agents can be used by detonating a homemade small bomb, or, as Aum Shinrikyo attacked in the Tokyo Metro Stations in Japan in 1995, by passively dispersing them into the air through a hole made in a plastic bag with an umbrella tip. Other factors that change the use and effectiveness of CWs are also weather conditions. The intensity of sunlight, heat, wind, and whether the weather is rainy are important. These hazardous agents can be persistent or volatile in the environment they are released into. The route of entry into the body is mainly through respiration, eyes, skin absorption, and digestion.[7,8]

For any toxic substance to be considered a CW in a military context, it must possess certain characteristics as follows:

1 It should have high toxicity.
2 It should be colorless, odorless, and heavier than air.
3 Its structure should not be easily damaged.
4 It should not be easily held by masks.
5 It must be resistant to air, water, and chemical substances.
6 The mode of action, protective measures, and treatment methods should not be known.
7 It should be easy and cheap to produce.
8 It should be usable and transportable after the necessary precautions have been taken.

Historical Context and Development of CWAs

Historians say that the first time such kind of weapons were used by the Chinese was in 1000-BC when arsenical smoke was used on the battlefield. Later on, Solon of Athens put hellebore roots in the drinking water of Kirrha in 600 BC. During the Peloponnesian war (429-424 BC) between the two leading City-States in ancient Greece (Athens and Sparta), Spartans created toxic gas by burning sulfur and releasing the toxic gas against their enemies. About 200 BC, the Carthaginians used Mandrake root left in the wine to sedate their enemies as well. Then in 256, Sassanians used crystal sulfur against the Romans in the city of Dura-Europos (Dura-Europos was an important trading center in Roman Syria.), and consequently, they conquered the city.[9–11]

Since the Peloponnesians used poisonous gas against the Spartans in 429 BC, poisons and chemicals have been used as weapons. The 1675 Strasbourg Agreement was the beginning of the first attempts to outlaw chemical weapons, which are now highly discussed as popular weapons. Germany and France signed it. Both sides have committed to forbidding the use of poisoned bullets under this agreement. In Europe, parallel to the development of modern chemistry in the 18th century, there was an increase in the production of synthetic chemical substances in many countries, especially Germany, and modern CWs emerged as a result of this development. The 20th century witnessed the rise in significance of chemical weapons during a period of heated debate about their use or non-use in combat. As a result of the use of chemical weapons in World War I (WWI), approximately 1.5 million people were injured and 90,000 people lost their lives. Germany deployed 180,000 kg of mustard and chlorine gas as CWs at Ypres, Belgium, in April 1915. Just before World War II (WWII), the development of nerve agents gave CWs an even more terrifying power. However, nerve agents were not used in World War II. Italy used the same gas in Ethiopia in 1930, and Japan used it against China in World War II. at 1988, during the Iran-Iraq war, CWs were deployed at Halabja, leading to the deaths of five thousand people. However, the events in our neighbour Syria and Israel's widespread use of white phosphorus in Gaza have brought chemical weapons to the attention of the world lately (Table 1).[7,8,12,13]

Clinical and Research Consequences

Nerve Agents: These are often considered the most lethal CWAs. Nerve agents are organophosphate (OP) compounds that irreversibly inhibit acetylcholinesterase (AChE), an enzyme essential for breaking down the neurotransmitter acetylcholine (ACh) at nerve synapses.[14] By blocking AChE, nerve agents cause a dangerous accumulation of acetylcholine in nerve endings. The result is continuous overstimulation of muscles, glands, and the central nervous system – a condition known as a cholinergic crisis. Nerve agents exert their lethal effects by irreversibly inhibiting acetylcholinesterase, resulting in the accumulation of acetylcholine and leading to paralysis and respiratory failure.[14]

Acute symptoms (the "SLUDGE" syndrome) include Salivation, Lacrimation (tearing), Urination, Defecation, Gastrointestinal distress, and Emesis (vomiting), along with pinpoint pupils, profuse sweating, muscle twitching, and convulsions. Victims typically experience bronchospasm and copious airway secretions (causing breathing difficulty), bradycardia (slow heart rate), and paralysis. Without rapid treatment, death often occurs by respiratory failure – due to paralysis of the diaphragm and other breathing muscles, compounded by bronchial constriction and seizure-induced hypoxia.[15] The onset of nerve agent effects can be seconds to minutes for volatile agents like sarin (especially if inhaled) or minutes for less volatile agents or dermal exposure. For example, inhaled sarin or VX vapor can cause fatal symptoms within 1–10 minutes at high concentrations. If exposure is via skin (especially for persistent agents like VX), onset might be delayed 10–30 minutes, but the outcome is equally lethal. Notably, nerve agents are rapid-acting – sarin's LCt50 (concentration × time product lethal to 50% of those exposed via inhalation) is only a few hundred mg·min/m^3. Physiologically, nerve agents affect both peripheral nerves (causing muscle fasciculations, paralysis) and the central nervous system (causing anxiety, convulsions, central respiratory depression). Seizures triggered by nerve agents can lead to permanent brain damage if prolonged.[15] Some nerve agents (notably the Novichok class) may have additional toxic effects beyond classical AChE inhibition, possibly interacting with other enzymes or receptors.[16]

Table 1. A chronological table of chemical warfare agent (CWA) use including major incidents involving toxic industrial chemicals (TICs) from the last century until today

Year	Location	Incident type	Notes on use
1915	Ypres, Belgium	CWA	First large-scale use of phosgene and chlorine gas by Germany in WWI
1917	Various locations, Europe	CWA	Widespread use of mustard gas by both sides in WWI (tens of thousands deaths and ~1.3 million injuries in total)
1921–1927	Rif, Morocco	CWA	Spain and France used chemical weapons against Rif rebels (Thousands of deaths)
1932	Hamburg, Germany	TIC	Destruction of a chemical plant released toxic gas (~1,000 deaths)
1935–1936	Ethiopia	CWA	Italy used mustard gas during the Second Italo-Ethiopian War (~15,000 deaths)
1940–1945	Nazi concentration camps, Europe	CWA	Nazis used Zyklon B (a cyanide-based pesticide) for mass executions (~1 million+ estimated deaths)
1943	Bari, Italy	CWA	German airstrike hit U.S. mustard gas stockpile, causing exposure (~83 deaths and ~600 injured)
1947	Ludwigshafen, Germany	TIC	Chemical plant explosion released toxic gases (207 deaths and ~3,800 injured)
1963–1967	Yemen	CWA	Egypt used mustard and nerve agents in the North Yemen Civil War (~1,500+ deaths)
1975–1988	Laos, Cambodia, Afghanistan	CWA	Alleged Soviet use of "yellow rain" mycotoxins
1976	Seveso, Italy	TIC	Dioxin (TCDD) released from chemical plant explosion (~2000 injured)
1980–1988	Iran-Iraq War	CWA	Iraq used mustard gas and nerve agents against Iran (~50000 deaths and ~100000 injured)
1984	Bhopal, India	TIC	Accidental release of methyl isocyanate (MIC) from Union Carbide plant (estimated number of people died in the first few days ranged up to 10,000)
1988	Halabja, Iraq	CWA	Iraq used sarin, VX, and mustard gas against civili-ans (~5000 deaths and ~10000 injured)
1994	Matsumoto, Japan	CWA	Aum Shinrikyo cult released sarin gas (7 deaths and ~600 injured)
1995	Tokyo, Japan	CWA	Aum Shinrikyo carried out sarin gas attack in subway (12 deaths and ~5500 injured)
2001	Toulouse, France	TIC	Fertilizer plant explosion released ammonia and chlorine gas (31 deaths and ~2500 injured)
2012–2018	Syria	CWA	Multiple chemical attacks, including sarin, mustard and chlorine gas (~1500–2000 deaths and ~10000 injured)
2013	West, Texas, USA	TIC	Fertilizer plant explosion released ammonia (15 de-aths and ~260 injured)
2017	Kuala Lumpur, Ma-laysia	CWA	Kim Jong-nam assassinated using VX nerve agent
2018–2020	Amesbury, UK and Moscow, Russia	CWA	A former Russian Military intelligence officer, and a Russian opposition leader were posoned with No-vichok nerve agent in 2018 and 2020, respectively
2020	Beirut, Lebanon	TIC	Ammonium nitrate explosion released toxic fumes (218 deaths and ~7000 injured)

CWA: Chemical warfare agent; TIC: Toxic industrial chemical; WWI: World War I.

Survivors of acute nerve agent poisoning can have lasting neurological deficits – for instance, some Tokyo sarin attack survivors showed Post-Traumatic Stress Disorder (PTSD) and EEG abnormalities even 5 years later.[17] In summary, nerve agents induce a catastrophic breakdown of normal neural signaling, and time-critical intervention is needed to prevent mortality.

Blister Agents (Vesicants): These chemicals (e.g., sulfur mustard, nitrogen mustard, lewisite) cause severe chemical burns to skin, eyes, and respiratory lining. Sulfur mustard (HD) is the best-known vesicant; it is a lipophilic alkylating agent that damages DNA, proteins, and cell membranes. Upon contact, mustard gas rapidly penetrates cells and undergoes intramolecular cyclization to form a

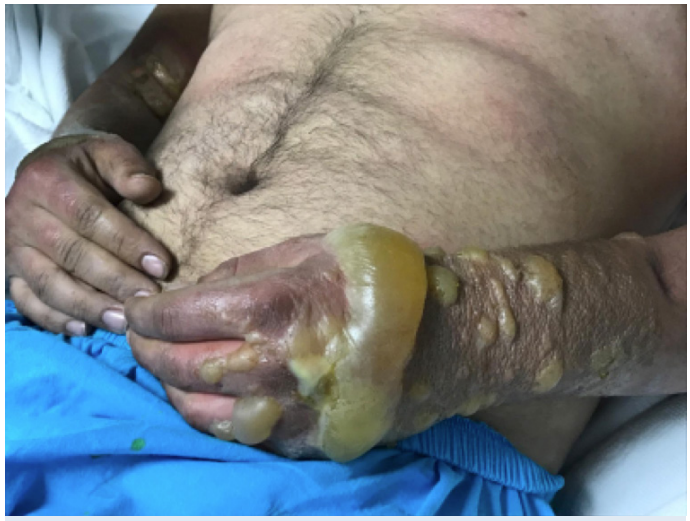

Figure 1. A photo of the sulfur mustard victim evacuated from the Syrian war and treated at Gaziantep Hospital, Türkiye, where the author served as the attending physician. The image which is from the archive of the author depicts extensive blistering and dermal injury on the arm and hand of a patient exposed to sulfur mustard (mustard gas). Characteristic large, fluid-filled bullae and erythematous skin are visible, consistent with the vesicant effects of sulfur mustard (picture from the author's own archive).

highly reactive ethyleneimonium ion. This ion alkylates DNA strands, leading to miscoding, strand breaks, and apoptosis of cells.[14] Mustard also alkylates proteins and glutathione, depleting cellular antioxidant defenses. The combined result is cell death and tissue necrosis, plus robust inflammatory responses. Clinically, mustard causes blistering lesions on skin (especially warm, moist areas). The onset is delayed – although cellular damage begins within minutes of exposure, victims may not feel pain or see blisters until 4–24 hours later, when extensive damage has occurred. The skin forms large fluid-filled blisters (bullae) that easily become infected (Fig. 1). Eye exposure to mustard leads to severe conjunctivitis, corneal damage, and possible blindness. Inhalation of mustard vapors causes necrosis of the mucous membranes and airway lining, leading to bleeding, sloughing of airway tissue, and pulmonary edema; many WWI gas fatalities were due to secondary lung infections (bronchopneumonia) after mustard inhalation injury.[13] Lewisite (an arsenic-based vesicant) causes similar blistering but acts faster and also has a systemic arsenic poisoning component. Unlike mustard, lewisite's effects (immediate pain on contact) provide warning, and an antidote (British Anti-Lewisite, dimercaprol) exists for systemic arsenic effects. Mustard is a persistent oily liquid that can remain active for days in temperate conditions, posing ongoing risk. Mustard contamination of soil can render areas dangerous; chronic exposure is linked to elevated cancer risk (skin, respiratory tract) years later, due to DNA alkylation and mutagenesis. No specific antidote still exists for mustard – it is primarily managed by prompt decontamination and supportive care. The painful, incapacitating injuries from vesicants make them primarily casualty-producing weapons (disabling troops and overwhelming medical logistics rather than killing outright – as seen in WWI, where mustard caused many casualties but low lethality).[7,12]

Blood Agents (Cyanogens): "Blood agents" is a term for poisons that prevent the blood cells from utilizing oxygen, causing rapid asphyxiation at the cellular level. The classic agents are hydrogen cyanide (HCN) and cyanogen chloride (CK), which release cyanide ions. Cyanide also results from combustion of plastics (hence firefighters carry cyanide antidotes for smoke inhalation victims). Emergency providers often encounter cyanide in industrial accidents or fires rather than warfare, but it is indeed a CWA (France considered using HCN in WWI, and the US developed CK for possible use in WWII).[7,18] Cyanide primarily binds to the iron atom in cytochrome c oxidase, an enzyme in the mitochondria responsible for the final step of the electron transport chain in aerobic respiration. By inhibiting cytochrome oxidase, cyanide halts cellular oxygen utilization (even if oxygen is present in the blood, cells cannot use it to produce ATP). This results in cytotoxic hypoxia – effectively, "internal asphyxiation." The brain and heart, with high oxygen demand, are most sensitive. Symptoms include rapid breathing, dizziness, nausea, headache, and a sense of suffocation. Victims develop severe metabolic acidosis (as cells switch to anaerobic metabolism and generate lactic acid). High doses lead to seizure, loss of consciousness, and cardiac arrest within minutes. Hydrogen cyanide is a volatile liquid (boiling point ~26 °C), so it is mainly a respiratory threat (inhalation), while cyanogen chloride is a gas that also can cause irritation (it has choking agent properties and can release HCl as well as cyanide). Cyanide acts extremely fast – it was used as a lethal execution gas (as HCN) because inhalation can kill in under 1 minute at high concentration. Blood agent poisoning is identified by rapid onset of collapse, "cherry-red" skin coloration (from high oxygenated blood that cells can't use), and the smell of bitter almonds (which not everyone can detect genetically).[7,19] Blood agents do have effective antidotes if given immediately. The traditional cyanide antidote kit uses amyl nitrite (inhaled) and sodium nitrite (IV) to induce methemoglobinemia – the nitrite converts some hemoglobin's iron from Fe^{2+} to Fe^{3+}, creating methemoglobin, which binds cyanide ion and pulls it off

cytochrome oxidase. This frees the enzyme to resume respiration. Sodium thiosulfate is then given IV; it provides sulfur donors that help the liver enzyme rhodanese convert cyanide to thiocyanate, which is excreted. A newer antidote, hydroxocobalamin (vitamin B_{12a}), directly chelates cyanide to form cyanocobalamin (vitamin B_{12}). Hydroxocobalamin (5 g IV infused over 15 min) can rapidly reverse cyanide poisoning and has the advantage of not inducing methemoglobin (so it preserves oxygen carrying capacity). Furthermore, research is ongoing into fast, intramuscular antidotes for mass-casualty use: one example is cobinamide, a compound related to cobalamin but with even higher cyanide affinity, which could be administered via auto-injector. In sum, blood agents kill by cutting off cells' ability to use oxygen; with prompt antidotal therapy, this process can be countered, but without treatment, death occurs in minutes.[20 21]

Choking Agents (Pulmonary Agents): These are gases or vapors that injure the respiratory tract, causing airway inflammation and fluid build-up in the lungs (pulmonary edema). The prototypical choking agents are chlorine (Cl_2) and phosgene ($COCl_2$), both used extensively in WWI. Choking agents react with the moist surfaces of the eyes, nose, throat, and lungs to form corrosive acids or other irritants. Chlorine, a green-yellow gas, reacts with water in mucous membranes to form hydrochloric acid (HCl) and hypochlorous acid. This causes instant irritation: burning of the eyes, throat, and a choking sensation. High concentrations lead to laryngospasm and reflex closure of airways, or direct acute lung injury.[8,22] Phosgene, a colorless gas with odor of cut hay, is insidious – it has about 6× the density of air and can accumulate in trenches or low areas. Phosgene reacts slower with water, producing HCl and carbon dioxide in the deep lung. Its primary injury is to the alveoli (air sacs) and capillaries: it acylates proteins and cell membranes in the alveolar walls disrupting the blood-air barrier. Phosgene causes little immediate irritation (so victims may inhale significant amounts unknowingly). After a delay of 2–24 hours, a severe non-cardiogenic pulmonary edema develops leading essentially the lungs slowly fill with fluid, impairing gas exchange.[23] Victims initially feel fine or only mild cough, but later suffer chest tightness, extreme shortness of breath, and cyanosis as pulmonary edema sets in. Chest X-ray shows fluffy infiltrates ("white-out") as fluid accumulates. This latent period made phosgene especially feared in WWI, as soldiers exposed would often only collapse hours after the attack during exertion or evacuation. Choking agents cause diffuse damage to the respiratory epithelium and endothelium. Autopsies from WWI phosgene casualties showed charred bronchial linings and waterlogged lungs. If a person survives the acute phase, there is risk of chronic lung fibrosis or reactive airway dysfunction. There is no specific antidote for choking agents; management is supportive – provide oxygen, bronchodilators (for reactive airway), and if needed mechanical ventilation with PEEP to manage pulmonary edema. Some animal studies indicate that certain treatments (e.g., aerosolized bicarbonate, or therapies targeting inflammation) have limited efficacy. For example, pulmonary injury from chlorine involves inflammation and oxidative damage, so antioxidants or corticosteroids have been tested as countermeasures, but results are mixed. In field scenarios, rapid removal from exposure and decontamination (fresh air, irrigation of eyes with water) is crucial. Emergency health responders may use nebulized bronchodilators or even inhaled bicarbonate to neutralize HCl in lungs, though the latter's benefit is unproven. Overall, choking agents incapacitate by essentially "drowning" the victim in their own fluids. For instance, fatal phosgene inhalation can produce fulminant pulmonary edema within 12–24 hours, which is why close monitoring of exposed individuals for delayed onset symptoms is essential. Chemical pulmonary agents also highlight the importance of protective masks – a simple gas mask can filter chlorine or phosgene and prevent the poisoning entirely, which is why these agents lost utility once armies were equipped with effective respirators.[5,7,23]

Incapacitating Agents: Unlike the above classes, incapacitating agents are designed not to kill but to cause temporary disability, disorientation, or unconsciousness. These include various chemicals affecting the central nervous system. One of the most infamous is 3-Quinuclidinyl Benzilate (BZ), a potent anticholinergic compound (similar to an extremely strong form of atropine or scopolamine).[24] BZ blocks acetylcholine receptors (particularly muscarinic receptors) in the brain, leading to anticholinergic syndrome – delirium, hallucinations, mydriasis (dilated pupils), dry mouth, elevated heart rate, urinary retention, and elevated body temperature. BZ was developed as a military incapacitant in the 1960s since the victim becomes confused, unable to coordinate, and often hallucinate for hours to days. Its onset is delayed (0.5–2 hours after exposure) and effects can last days.[5] Other incapacitating agents tested or used include fentanyl derivatives or other opioids (which cause unconsciousness or respiratory arrest – suspected in the Moscow theater

Table 2. Evidence and signs indicating the use of chemical weapons at the incident site

Unusual occurrence of dead or dying animals (like dead birds)
Unexplained casualties (multiple victims with similar signs and symptoms)
Unusual liquid or vapour (droplets, unexplained odour)
Suspicious dispersal devices or packages (spray devices and munitions)
Data suggesting a massive point-source outbreak
High morbidity and mortality relative to the number of personnel at risk
Multiple disease entities in the same patients
Sudden appearance of a disease that is unusual or that does not occur naturally in a certain geographic area

2002 incident when Russian forces released a fentanyl-based gas to subdue hostage-takers, albeit with lethal consequences for many hostages), as well as psychotropic agents (LSD was briefly considered as a warfare agent).[25] For BZ and other anticholinergic delirients, the antidote is physostigmine, a cholinesterase inhibitor that can increase acetylcholine levels to outcompete the receptor blockade. Physostigmine can reverse delirium if administered carefully, although the effect is temporary (BZ's duration is long). Supportive care (cooling, hydration, sedation) is also used. Incapacitants blur the line between CWs and riot control agents or pharmaceutical chemicals – their intent is to disable without permanent harm, but in practice the distinction is murky and the CWC bans their use in warfare. For instance, the fentanyl gas used in 2002 was technically a pharmaceutical opioid, not explicitly listed as a CWA, but its use as a weapon had lethal outcomes. Incapacitants remind us that any potent bioactive chemical can be a weapon if misused. Emerging "non-lethal" agents (calmatives, convulsants, etc.) continue to be of concern in security circles.[26]

Summary of Overall Effects: Generally speaking to summarize, each class of CWA targets a critical biological process – nerve agents shut down neurotransmission, blister agents destroy tissues, blood agents halt cellular respiration, choking agents cripple the lungs, and incapacitating agents disrupt the mind. The physiological effects range from immediate (nerve, blood, choking) to delayed (blister, some incapacitating) and from largely reversible (incapacitants) to often permanent or fatal. Understanding these mechanisms guides the detection (since many detection methods sense the chemical or its effects on biosensors), protection (choosing the right filters or antidotes), and medical treatment (e.g., using atropine for nerve agent, or nitrites for cyanide, etc.). It also underscores why rapid identification of the agent is vital during an incident – different CWAs require very different emergency responses.[27]

Medical CBRN Response Against Chemical Attacks

In the event of an attack due to or in any preparation for a chemical CBRN attack, main components and steps of the medical CBRN defense to be developed can be summarized as follows:

a The development or update of medical intelligence and health surveillance systems,

b The development of early and advanced diagnostic systems,

c Procurement and development of protective equipment and systems,

d Standarization of first aid and treatment activities,

e Planing and performin the medical CBRN training,

f Establishment of effective health organization and planning.

a. Development of Intelligence and Medical Surveillance Systems: It is of great importance to properly maintain health statistics and relevant records in revealing exposure to CWAs, which are also weapons of mass destruction. In this context, the evaluation of epidemiological data and the development and implementation of national and international monitoring policies to track the activities of individuals, terrorist groups, and states that may produce and use of chemical agents are strategically necessary.

b. Development of early and advanced detection systems: The rapid detection of CBRN chemical agents and the necessary alerts regarding this matter, as well as rapid administration of appropriate protective measures and treatment against the agents, are important and should be carried out promptly. In the event of an incident, certain indicators written in Table 1 in the incident area suggesting the use of an CBRN Chemical agent will raise our suspicion of an chemical attack, and they possess characteristics that will be confirmed by results obtained through various diagnostic methods (Table 2).[28]

Detection procedures are examined under two main headings:

(1) Detection procedures that can be applied in areas contaminated with CBRN agents (on-site detection),

(2) Detection of samples contaminated with CBRN agents using advanced methods by reference laboratories (off-site detection).

These detection processes should be carried out using various biological and environmental samples. For this purpose, the establishment of specialized CBRN Sample Collection and Detection teams is of great importance in medical CBRN defense. These teams should be properly equipped, possess procedures for sample collection and transport, and have communication capabilities both internally and with the laboratory to which the sample will be sent. It is also considered beneficial for the personnel in sample collection and detection teams to undergo training and drills for the effective execution of their duties.[29]

In the samples taken, the detection of the agent should be carried out either in mobile CBRN Laboratories equipped with the necessary equipment to provide a diagnosis in the shortest time possible in the field, or in reference laboratories located at a greater distance but equipped with advanced technology devices and more experienced personnel. Detection operations in field conditions can be carried out using different devices and techniques depending on the chemical properties of the agent used. Reference laboratories are accredited laboratories where the confirmation of preliminary diagnoses, as well as scientific research and project work on the diagnosis, treatment, and protection against CWAs, are conducted. They should be considered leading institutions in providing advanced Medical CBRN training to healthcare personnel.

c. Procurement and development of protective equipment and systems: To effectively defend against CWAs, it is necessary to be aware of personal and collective protective measures including protection against the release of CWs, procurement these materials, development of appropriate medical defense systems, and having sufficient information about their use.[5,8]

(1) Personal Protection: Personal protection measures include the use of protective masks and protective clothing. Protective mask is such a material that protects the face, eyes, and respiratory tract from toxic agents and cleans the air contaminated with these substances. Masks filter the inhaled air through a carbon filter with high adsorption capacity before inhaling. The protection provided by gas masks depends on how early the staff and the public is alerted, how properly the mask is worn, and the properties of the material that makes up the filter, causing preventing or significantly reducing the onset of lethal effects that could occur in a very short time due to the exposure. The personal protective suit, on the other hand, is used primarily to prevent the agent from coming into contact with the skin. The protective suit should provide at least 6 hours of protection in a densely chemical release environment according to NATO standards. After putting on the suit, gloves and boots should be worn, and a mask should be put on.[5,30]

(2) Collective Protection: Especially shelters are collective protection areas for both soldiers and civilians. It is necessary to install appropriate, safe, and adequate ventilation and filtration systems in these closed areas. In places where there are no shelters, measures such as preparing a room within the house as a shelter, taping the window and door frames with thick tape, and covering them with plastic sheeting to prevent outside infiltration can also be taken. In such shelters, there should be 1.5–3 m^3 of ventilable air for each person. The minimum oxygen level required in the environment should be between 13–15%, and it should be considered that this value can be reached within 6–8 hours with an area of 0.75 m^2 and a ceiling height of 2.2 meters.[31]

d. First aid and treatment approach:

(1) At first hand, it is essential to provide the establishment of first aid and treatment teams and set-up in healthcare facilities, and the preparation and implementation of medical response plans. In this context, a medical chemical CBRN treatment is evaluated in two phases: in field conditions and in hospital conditions.

(a) Medical Chemical First-aid and Treatment in Field Conditions: A casualty exposed to a CWA is either sent to the decontamination area or directly to the hospital. When the injured person is sent to the decontamination area, decontamination procedures should be applied there, and then they are sent to the first aid station in the cold zone. After the injured person is brought to the first aid station, he is evaluated and examined by medical personnel, and required medical treatment is immediately initiated according to the nature of the case. Again, the triage is conducted here, and the transfer of cases that need to be sent to a more equipped healthcare institution is carried out under appropriate conditions as soon as possible.

(b) Treatment in Hospital Conditions: Treatment in hospital conditions varies depending on whether the personnel who have been in contact with CWAs have undergone decontamination procedures before arriving at the hospital and whether they have received treatment. For chemical

Table 3. Antidotal treatment available for the chemical warfare agents

Agents	Antidote	Dosage
Nerve agents	Atropine	2–8 mg IM/IV. Full atropinization maintained at 2 mg doses every 3–8 min for several hours
	Pralidoxime	1–2 g IV (0.5 g/min) in saline
	Diazepam (valium)	5–10 mg IV/IM/p.o.
	Pyridostigmine bromide	30 mg every 8 h
Lewisite	BAL (dimercaprol)	Commercial preparation of %10 BAL in pe-anut oil up to 4.0 ml IM. Repeat in 4, 8, 12 h
	BAL analogues (DMPS, DMSA, DMPA)*	DMSA 300 mg orally every 6 h for 3 days.
Hydrogen cyanide	Amyl nitrite	Inhaled for 30 s/min and maintained until the initiation of Na nitrite
	Sodium nitrite	IV infusion of 10 ml over 3–5 min
	Sodium thiosulphate (25 %)	IV infusion of 50 ml
	4-DMAP (4-Dimethylaminophenol)	3 mg/kg IV injection
BZ (incapacitant)	Physostigmine	2 mg in 10 ml saline IV (over 5 min)

*DMPS: 2,3-Dimercapto-1-propanesulfonic acid; DMSA: Dimercaptosuccinic acid; DMPA: Dimercaptopropanol acetate.

casualties who arrive at the hospital without any intervention, decontamination should be performed in a separate decontamination room prior emergency department or in a mobile decontamination unit stationed prior to the emergency department. After the decontamination process is confirmed positively, the casualty is accepted to the emergency department in safe. In the emergency department, personnel equipped with appropriate protective gear (physicians, nurses, other clinical service staff, etc.) has to evaluate the injured person in details followed by the required medical urgent interventions. Although it has been notified that the injured patients who have undergone decontamination and received initial treatment before arriving at the hospital have to get undergone a confirmatory contamination check and decontamination status as a precaution. If it is determined that adequate decontamination has not been achieved as a result of the control procedure, the patient will undergo decontamination again. After receiving the injured patient, appropriate diagnosis and treatment procedures are applied (Table 3). As a precaution against the possibility of the number of injured exceeding the emergency department's capacity, other concerned clinics or units of the hospital including ICU and trauma clinics should be alerted in advance.

(2) Procurement of drugs, medical supplies, and equipment for first aid and treatment: In the event of an attack with CWAs, medical rescuers and healthcare providers must also consider first aid and treatment approaches in the overall evaluation of contaminated casualties. Elementary vital functions should be aggressively supported and ABC (Airway, Breathing and Circulation) should be corrected.

Figure 2. The image illustrates a decontamination process which is a critical component in the medical management of chemical weapon exposure. Victims are undergoing systematic decontamination through water showers, assisted by trained personnel in personal protective suit ensuring the effective removal of residual chemical agents. This photo was taken from the archive of the author who led medical CBRN exercise as part of a training program designed to enhance preparedness for chemical emergencies.

Antidotal therapy is not concerned for either CWA.[7] The antidotal regimen recommended for a chemical casualty is given in Table 3.

(3) Establishment of decontamination systems: Decontamination is the process of reducing or eliminating the contamination of personnel, vehicles, equipment, and terrain resulting from exposure to chemical warfare agents using various methods and substances (Fig. 2). A 0.5% solution of hypochlorite (one part household bleach to

Table 4. Categories of triage used in classification of chemical casualties

T1 (immediate):	Casualties who require medical care and advanced life support within a short time on the incident site and further in the hospital.
T2 (delayed):	Casualties with injuries who are in need of prolonged care and require hospitalization. Delay of this care does not affect the prognosis of the in-jury negatively.
T3 (minimal):	Casualties who have minor injuries who will not be evacuated and will be able to return to duty in a short time.
T4 (expectant):	Casualties with fatal injuries who will possibly not survive with standard medical care.

nine parts water) should be gently applied and rinsed off with water at the last station. That rubbing and scrubbing the skin may sometimes enhance the agent absorption must be kept in mind. The decontamination process is divided into two based on the location of execution.

• Decontamination at the scene

• Decontamination in the hospital

The decontamination process is divided into four levels.

- Personnel Decontamination
- Vehicle and Equipment Decontamination
- Field Decontamination
- Wounded Decontamination

(4) On-site and post-incident triage procedures: Triage is the process of categorizing the injured according to the priority of medical care and the available medical resources. In an attack due to CWAs, the triage process begins from the first encountering with the patient and is a dynamic process that continues at every stage of the medical approach. Triage is performed periodically and repeated in case of any changes in the patient's clinical signs and medical capabilities. In the triage process, the triage officer will carefully evaluate the symptoms indicating the respiratory, neurological, and circulatory status of the injured to prevent the overwhelming of healthcare facilities. The triage staff should primarily be assigned from amongst emergency medicine specialists, experienced surgeons, or internal medicine specialists. The responsibilities of the triage officer include knowing the natural course and prognosis of the injury, being aware of the status of existing medical support conditions (personnel status, hospital capabilities of beds, medicines, antidotes, ICU, etc), determining the status of the current and projected patient flow over time, having precise knowledge of medical evacuation capabilities, and being able to distinguish those who have experienced psychological trauma or worried-well patients. The triage system commonly used by medical units includes four categories that are based on the need for medical care: immediate, delayed, minimal and expectant (Table 4).[8,32]

Conclusion

The growing risk of CBRN attacks, especially from the Middle East, shows the need for strong medical CBRN defense systems. This paper is to highlight the importance of improving health monitoring, early detection, and emergency response. Having the right protective gear and meeting safety standards, like ensuring enough fresh air and oxygen in shelters is crucial. Clear steps for first aid, decontamination, and treatment help save lives in chemical attacks, while proper training for healthcare workers boosts readiness. Working together globally, improving detection tools, and planning well-organized health services are key to staying prepared for CBRN threats.

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References

1. Ekzayez A, Flecknoe MD, Lillywhite L, Patel P, Papamichail A, Elbahtimy H. Chemical weapons and public health: Assessing impact and responses. J Public Health (Oxf) 2020;42(3):e334-42. [CrossRef]
2. Kenar L. Kimyasal savaş ajanlarının genel özellikleri, tarihçesi ve tehdidi. Turkiye Klinikleri CBRN-Special Topics 2023;1(1):1-6. [in Turkish]
3. Arms Control Association. Chemical and biological weapons status at a glance. Available at: https://www.armscontrol.org/factsheets/cbwprolif. Accessed March 7, 2025.
4. Madsen JM, Darling RG. Future biologic and chemical weapons. Disaster Medicine 2006;424-33. [CrossRef]
5. Kenar L. Establishment of "National NBC defence and first-aid system" for our country against an NBC attack. Dissertation, Ankara: GATA; 2002.
6. DeLuca MA, Chai PR, Goralnick E, Erickson TB. Five decades

of global chemical terror attacks: Data analysis to inform training and preparedness. Disaster Med Public Health Prep 2021;15(6):750-61. [CrossRef]
7. Ortatatli M, Kenar L, Arora R, Arora P. Role of military hospitals in handling chemical and biological disasters. In: Disaster management: Medical preparedness, response and homeland security. Wallingford (UK): CABI; 2013:275-310. [CrossRef]
8. Hancı M, Uzan M. Gün Sıfır Travmatoloji. İstanbul: Nobel Tıp Kitabevleri; 2013:461-511.
9. Mayor A. Greek fire, poison arrows & scorpion bombs: Biological and chemical warfare in the ancient world. New York: Overlook Press; 2003.
10. James S. Stratagems, combat, and "chemical warfare" in the siege mines of Dura-Europos. Am J Archaeol 2011;115:69-101. [CrossRef]
11. Hasegawa GR. Proposals for chemical weapons during the American Civil War. Mil Med 2008;173:499-506. [CrossRef]
12. Kilic E, Ortatatli M, Sezigen S, Eyison RK, Kenar L. Acute intensive care unit management of mustard gas victims: The Turkish experience. Cutan Ocul Toxicol 2018;37:332-7. [CrossRef]
13. Sezigen S, Kenar L. Recent sulfur mustard attacks in Middle East and experience of health professionals. Toxicol Lett 2020;320:52-7. [CrossRef]
14. Cruz-Hernandez A, Roney A, Goswami DG, Tewari-Singh N, Brown JM. A review of chemical warfare agents linked to respiratory and neurological effects experienced in Gulf War illness. Inhal Toxicol 2022;34:412-32. [CrossRef]
15. Chambers JE, Dail MB, Meek EC. Oxime-mediated reactivation of organophosphate-inhibited acetylcholinesterase with emphasis on centrally-active oximes. Neuropharmacology 2020;175:108201. [CrossRef]
16. Charejoo A, Arabfard M, Jafari A, Nourian YH. A complete, evidence-based review on Novichok poisoning based on epidemiological aspects and clinical management. Front Toxicol 2023;4:1004705. [CrossRef]
17. Yanagisawa N, Morita H, Nakajima T. Sarin experiences in Japan: Acute toxicity and long-term effects. J Neurol Sci 2006;249:76-85. [CrossRef]
18. Parker-Cote JL, Rizer J, Vakkalanka JP, Rege SV, Holstege CP. Challenges in the diagnosis of acute cyanide poisoning. Clin Toxicol 2018;56:609-17. [CrossRef]
19. Leavesley HB, Li L, Prabhakaran K, Borowitz JL, Isom GE. Interaction of cyanide and nitric oxide with cytochrome c oxidase: Implications for acute cyanide toxicity. Toxicol Sci 2008;101:101-11. [CrossRef]
20. Baskin SI, Horowitz AM, Nealley EW. The antidotal action of sodium nitrite and sodium thiosulfate against cyanide poisoning. J Clin Pharmacol 1992;32:368-75. [CrossRef]
21. Borron SW, Baud FJ, Mégarbane B, Bismuth C. Hydroxocobalamin for severe acute cyanide poisoning by ingestion or inhalation. Am J Emerg Med 2007;25:551-8. [CrossRef]
22. Zellner T, Eyer F. Choking agents and chlorine gas-History, pathophysiology, clinical effects and treatment. Toxicol Lett 2020;320:73-9. [CrossRef]
23. Marzec J, Nadadur S. Countermeasures against pulmonary threat agents. J Pharmacol Exp Ther 2024;388:560-7. [CrossRef]
24. Misik J. Military incapacitating agent BZ (3-quinuclidinyl benzilate)-Past, present and future. Mil Med Sci Lett 2013;82:115-9. [CrossRef]
25. Riches JR, Read RW, Black RM, Cooper NJ, Timperley CM. Analysis of clothing and urine from Moscow theatre siege casualties reveals carfentanil and remifentanil use. J Anal Toxicol 2012;36:647-56. [CrossRef]
26. Pitschmann V, Hon Z. Drugs as chemical weapons: Past and perspectives. Toxics 2023;11:52. [CrossRef]
27. Coleman CN, Bader JL, Koerner JF, Hrdina C, Cliffer KD, Hick JL, et al. Chemical, biological, radiological, nuclear, and explosive (CBRNE) science and the CBRNE science medical operations science support expert (CMOSSE). Disaster Med Public Health Prep 2019;13:995-1010. [CrossRef]
28. Ciottone GR. Toxidrome recognition in chemical-weapons attacks. N Engl J Med 2018;378:1611-20. [CrossRef]
29. NATO Standardization Agency. NATO handbook for sampling and identification of biological, chemical and radiological agents (SIBCRA). Edition A, Version 1. Brussels: NATO Standardization Agency; 2015.
30. NATO Standard AEP-38 Oerational Requirements, Technıcal Specifications and Evaluation Criteria for CBRN Protectıve Clothing Volume I Edition C, Version 1 MARCH 2021 www.nato.int
31. Smilowitz R, Blewett W, Williams P, Chipley M. Risk management series: Safe rooms and shelters. Washington (DC): US Department of Homeland Security, FEMA; 2006.
32. Kenar L, Eryılmaz M. Evaluations on triage applications for chemical casualties in chemically contaminated area. JAEM 2009;8:9-13. [CrossRef]