

History of chemical and biological warfare agents

L. Szinicz*

Bundeswehr Institute of Pharmacology and Toxicology, Neuherbergstr. 11, D-80937 Munich, Germany

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Abstract

Chemical and biological warfare agents constitute a low-probability, but high-impact risk both to the military and to the civilian population. The use of hazardous materials of chemical or biological origin as weapons and for homicide has been documented since ancient times. The first use of chemicals in terms of weapons of mass destruction goes back to World War I, when on April 22, 1915 large amounts of chlorine were released by German military forces at Ypres, Belgium. Until around the 1970s of the 20th century, the awareness of the threat by chemical and biological agents had been mainly confined to the military sector. In the following time, the development of increasing range delivery systems by chemical and biological agents sensitised public attention to the threat emanating from these agents. Their proliferation to the terrorists field during the 1990s with the expanding scale and globalisation of terrorist attacks suggested that these agents are becoming an increasing threat to the whole world community. The following article gives a condensed overview on the history of use and development of the more prominent chemical and biological warfare agents.

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1. Introduction

Hazardous materials of chemical and biological origin have been part of evolution and have been used as weapons and for homicide since prehistoric times. Their use in warfare has been reported since ancient Greek and Roman times, even if their impact had been comparatively limited due to the restricted knowledge at that time. During the 19th century, rapid advances in chemistry and the development of the chemical industry were accompanied by grievous accidents with hazardous chemicals. Increasing knowledge on their toxicological effects and the possibility for large-scale production of hazardous chemicals provided the basis for their first use

as weapons of mass destruction during World War I. This event also marked the beginning of continuously growing efforts to develop more and more effective chemical agents, hazardous toxins and microorganisms including appropriate delivery systems for their usage in warfare. While in these times the awareness of the threat by chemical and biological warfare agents was confined to the military field, the development of long-range delivery systems by several chemical and biological weapon possessors promoted the perception of a new dimension of threat also for civilian population. The proliferation of these agents to the terrorist field during the 1990s and the globalisation and escalation of terrorist attacks in recent times resulted in a common awareness of the necessity to include this threat in national and international emergency and risk management plans. A condensed overview on the history of use and development of chemical and biological weapons is given below.

* Tel.: +49 89 3168 2925; fax: +49 89 3168 2333.

E-mail address: Ladislausszinicz@bundeswehr.org.

A complete historical overview of the development and use of these agents would be far beyond the scope of this article. Deeper insight is given by Robinson and Leitenberg (1971), Robinson et al. (1973), Lewin (1920), Hanslian (1937), Smart (1997) and Joy (1997). Further information can also be found on the Internet page of the Center for Nonproliferation Studies (CNS). Major parts of this article were extracted from Robinson and Leitenberg (1971) and Robinson et al. (1973). Data, which are not specifically cited can be found in these extensive reviews on the topic.

2. Classification of biological and chemical weapons

Biological or chemical warfare agents can be microorganisms, toxins and chemicals, respectively, which are intended for use in military operations in order to kill, seriously injure or incapacitate exposed individuals by exerting their physiological effects. Chemical and biological weapons are the respective agents with their delivery systems.

A large number of microorganisms, toxins and chemicals have been investigated as potential biological or chemical agents. A common list of biological agents, which belong to the so-called “dirty dozen” is given in Table 1. The currently most important chemical agents are summarized in Table 2.

Table 1
Classification of biological agents

| Group, causative agent | Disease | Symbol ^a |
|---|--------------------------------|---------------------|
| Bacteria | | |
| <i>Bacillus anthracis</i> | Anthrax | – |
| <i>Yersinia pestis</i> | Plague | – |
| <i>Francisella tularensis</i> | Tularemia | – |
| <i>Brucella</i> spp. | Brucellosis | – |
| <i>Malleomyces pseudomallei</i> | Melioidosis | – |
| Rickettsiae | | |
| <i>Coxiella burnetii</i> | Q fever | – |
| Viruses | | |
| Variola virus | Smallpox | – |
| VEE virus | Venezuelan equine encephalitis | – |
| Marburg virus, Ebola virus | Hemorrhagic fever | – |
| Toxins | | |
| Botulinal toxins | Botulism | X |
| Ricin | Ricin poisoning | W |
| <i>Staphylococcal enterotoxin B</i> (SEB) | SEB poisoning | PG |

^a US Army symbols.

3. History of the use of chemical and biological agents

Poisonous compounds and dangerous microorganisms have been integral parts of evolution. Reports of man using fire and smoke, contaminating drinking water supplies with corpses or cadavers thereby spreading microorganisms and other poisonous agents or employing poisoned darts and other weapons go back to prehistoric times.

Compared to conventional weapons, relatively small amounts of modern chemical and biological agents may cause high numbers of casualties. Therefore, chemical and biological warfare agents have been classified as weapons of mass destruction. In WW I and II, their use was confined to military conflicts. The first chemical agents used in WW I were respiratory irritants. They were followed by the lung-damaging agents chlorine and phosgene. An increase of injured occurred after the introduction of sulphur mustard during WW I (injury not only by inhalation but also by skin exposure). A further increase of injuries and deaths would occur if nerve agents are used (very high toxicity after inhalation and cutaneous exposure). An important step forward towards an ever increasing threat by weapons of mass destruction was made by the development of long-range missiles, which can carry the threat to areas far away from the original conflict region. Further events, which suggested the proliferation of weapons of mass destruction had been the terror attacks in Matsumoto (1994) and Tokyo (1995). Both incidents were performed by a non-state organisation, i.e. the Aum Shinrikyo religious sect. This showed the increasing distribution of know-how with regard to the production and use of these agents. Finally, the events of September 11, 2001 have demonstrated the intention of terrorists to increase the scale of attacks and the number of victims.

3.1. Antique

600 B.C.—Helleborus roots (active ingredients: protoanemonin, steroidal saponines, bufadienolides; Frohne and Pfaender, 1997) were used successfully by the Athenian dictator Solon to contaminate water supplies during the siege of Kirrha (Smart, 1997).

431–404 B.C.—Usage of ignited pitch and sulphur by Spartans at Platea and Delium during the Peloponnesian War (Hanslian, 1937).

360 B.C.—Ainaias suggests the use of pots containing sulphur, resin, pitch, tow and wood chips (Hanslian, 1937).

Table 2
Classification of chemical agents according to their target organs or tissues

| Group/chemical name | Common name | Symbol ^a |
|--|------------------|---------------------|
| Nerve agents | | |
| Ethyl- <i>N,N</i> -dimethyl phosphoramidocyanidate | Tabun | GA |
| Isopropyl methyl phosphonofluoridate | Sarin | GB |
| Cyclohexyl methyl phosphonofluoridate | Cyclosarin | GF |
| Pinacolyl methyl phosphonofluoridate | Soman | GD |
| <i>o</i> -Ethyl- <i>S</i> -(2-diisopropylamino-ethyl)-methyl phosphonothiolate | – | VX |
| Vesicant agents | | |
| Bis(2-chloroethyl)sulfide (Yperite, S-Lost) | Sulphur mustard | H, HD |
| Tris(2-chloroethyl)amine | Nitrogen mustard | HN-3 |
| 2-Chlorovinyl dichloroarsine | Lewisite | L |
| Lung-damaging agents | | |
| Carbonyl chloride | Phosgene | CG |
| Trichloromethyl chloroformate | Diphosgene | DP |
| Blood agents | | |
| Hydrogen cyanide | – | AC |
| Cyanogen chloride | – | CK |
| Incapacitating psychochemicals | | |
| 3-Quinuclidinyl benzilate | – | BZ |
| Lacrimators | | |
| 2-Chloroacetophenone | – | CN |
| 2-Chlorobenzalmalononitrile | – | CS |
| Vomiting agents | | |
| Diphenylchloroarsine | Clark I | DA |
| Diphenylcyanoarsine | Clark II | DC |
| 10-Chloro-5,10-dihydrophenarsazine | Adamsite | DM |

^a US Army symbols.

190 B.C.—Hannibal hurls clay jars with venomous snakes onto ships of Pergamus at Eurymedon winning thereby the battle (Smart, 1997).

About 200 B.C.—Carthaginians use mandrake roots (active ingredients: tropane alkaloids, e.g. scopolamine, atropine) to spoil wine for sedating their enemies (Smart, 1997).

3.2. Middle ages

960–1279 A.D.—Usage of arsenic smoke in battles during China Sung Dynasty (Hersch, 1968).

1155 A.D.—Barbarossa employs cadavers to contaminate adversary water supplies in the battle of Tortona (Smart, 1997).

1346–1347 A.D.—Mongols (de Mussis) catapult plague-infected corpses over the walls of Kaffa (Crimea), forcing the besieged Genoese to flee (Smart, 1997). A plague pandemic in Europe is believed to have emerged from this event.

1495 A.D.—The Spanish tried to contaminate wine with blood from leprosy patients in order to defeat the French near Naples (Smart, 1997).

1452–1519 A.D.—Leonardo da Vinci proposes the use of smoke containing arsenic to lay siege to adversary fortifications (Lohs, 1989).

Circa 1570 A.D.—The Austrian Knight Veit Wulff von Senftenberg reports on Hunyadi using arsenical smoke when defending Belgrade against the Turks (Hanslian, 1937; Robinson and Leitenberg, 1971).

1650 A.D.—Polish general Siemienowicz puts saliva from rabid dogs into hollow spheres before firing them against the enemies (Smart, 1997).

1710 A.D.—The Russians manage to deposit plague-infected cadavers in the Swedish-held town of Reval, Estonia (Smart, 1997).

1763 A.D.—During the Pontiac's Rebellion in New England, the British (officer) Colonel Henry Bouquet proposed to distribute smallpox-infected blankets

to the Indians at Fort Pitt, Pennsylvania. While still remaining unclear whether this dissemination had been launched on purpose, the disease proved to be devastating to the native American population (Smart, 1997).

1785 A.D.—Tunisians deposited plague-infected clothing in La Calle, which at the time was being held by the Christians (Smart, 1997).

June 19, 1845 A.D.—1095 out of 1150 men of the Kabyl Tribe Ouled-Rhia die of suffocation in the cave of Nemchia after the French Colonel Pelissier had given the order to generate smoke by burning freshly cut wood (Hanslian, 1937).

3.3. Modern times

3.3.1. 1914–1918—World War I

August 1914—First use of the irritant ethylbromoacetate by French military Forces (Robinson and Leitenberg, 1971).

October 1914—First (and only) use of the sneezing agent *o*-dianisidine chlorosulphonate (Niespulver) by German Forces (Robinson and Leitenberg, 1971).

November 1914—First use of the irritant chloroacetone by French Forces shortly after being followed by Germany and Russia. Later on, many other irritants were used or were being tested by almost all belligerents until the end of WW I (Table 3) (Robinson and Leitenberg, 1971).

April 22, 1915—First use of the lung-damaging agent chlorine by German Forces in the attack at Ypres. This event marked the first large-scale use of a chemical agent with the intention to cause severe injury or death, therefore being classified as weapon of mass destruction (Robinson and Leitenberg, 1971).

December, 1915—First use of the lung-damaging agent phosgene by German Forces followed by usage of this agent by all other belligerents (Robinson and Leitenberg, 1971). During WW I most casualties (deaths) caused by exposure to chemical agents were due to phosgene or phosgene/chlorine mixtures.

July, 1916—First use of the so-called blood agent hydrogen cyanide by French Forces and shortly after by the United Kingdom and Russia (Robinson and Leitenberg, 1971).

October, 1916—First use of the so-called blood agent cyanogen chloride by French Forces (Robinson and Leitenberg, 1971).

July 10/11, 1917—First use of an arsenical sternutator – diphenylchloroarsine – by German Forces, followed by the use of phenyldichloroarsine in September 1917 and diphenylcyanoarsine in May 1918 (Masken-

brecher: Mask breaker) (Hanslian, 1937; Robinson and Leitenberg, 1971). After being released by burning, this type of agent formed very fine aerosols, which passed the common mask filters of that time.

July 12/13, 1917—First use of the skin damaging agent bis (2-chloroethyl) sulfide (sulphur mustard) by German Forces at Ypres, followed by further usage by France and the United Kingdom (Robinson and Leitenberg, 1971). This was the first agent used not only to act mainly via the lung but also at and through the skin. In these times, soldiers had only been staffed with respirators but not with skin protection devices. Consequently, the number of injuries due to chemical agents increased after introduction of this agent.

March, 1918—First use of the skin damaging arsenical agents ethyl- and methylchloroarsine by German Forces (Robinson and Leitenberg, 1971).

1935–1936—Italian invasion in Ethiopia: use of tear gas and mustard gas (Robinson and Leitenberg, 1971).

1937–1945—Japanese invasion in China: use of tear gas (chloracetophenone), sternutators (diphenylcyanoarsine), phosgene, mustard gas and lewisite (Robinson and Leitenberg, 1971).

1940–1944—Japanese invasion in China: use of cholera and plague (vector flees) against the civilian population of China and Chinese troops (Robinson and Leitenberg, 1971).

1940–1945—Concentration camps of the Third Reich: use of Zyklon B (cyanide adsorbed onto a powder base) (Robinson and Leitenberg, 1971).

1941–1942—Testing of aerial bombs and cannon shells for biological warfare: dissemination of anthrax spores at Gruinard Island, Scotland (Robinson and Leitenberg, 1971).

1963–1967—Egyptian intervention in Yemen: use of irritants and mustard gas (Robinson and Leitenberg, 1971).

1961–1970—US intervention in Indo-China (US Forces and South Vietnam Forces): use of irritants (2-chlorobenzalmalononitrile, CS) by US Forces. The South Vietnam Forces used *a*-chloracetophenone and adamsite. Use of defoliant chemicals by US Forces: agent purple, orange, white and blue containing various mixtures of *n*-butyl 2,4-dichlorophenoxyacetate (2,4-D), *n*-butyl 2,4,5-trichlorophenoxyacetate (2,4,5-T), *iso*-butyl trichlorophenoxyacetate, cacodylic acid or picloram (Robinson and Leitenberg, 1971). The chlorinated phenoxyacetate products were contaminated by dioxins as a production based impurity.

1978, September 7—Assault upon the exile Bulgarian Markov with an umbrella: use of Ricin (Harris and Paxman, 1982).

Table 3
Toxic chemicals, which have been considered as chemical warfare agents

| Chemical name | Common name/US code | Remarks ^a |
|---|---------------------|---|
| Antipersonnel agents | | |
| Irritating incapacitants | | |
| Ethyl bromoacetate | EBA | Minor lachrymator WW I/civilian use |
| Ethyl iodoacetate | | Major lachrymator WW I |
| Chloromethyl chloroformate | | Minor lachrymator WW I |
| Dichloromethyl chloroformate | | Minor lachrymator WW I |
| Chloroacetone | | Minor lachrymator WW I |
| Bromoacetone | BA | Most used lachrymator WW I |
| Bromomethylethyl ketone | | Major lachrymator WW I/civilian use |
| Iodo-acetone | | Minor lachrymator WW I |
| Acrolein | | Minor lachrymator WW I |
| <i>N</i> -Ethylcarbazole | | Minor agent WW I |
| Xylyl bromide | | Major lachrymator WW I |
| Xylilene bromide | | Major lachrymator WW I |
| Benzyl iodide | | Minor lachrymator WW I |
| <i>o</i> -Nitrobenzyl chloride | | Minor lachrymator WW I |
| <i>a</i> -Bromobenzyl cyanide | BBC (CA) | Major lachrymator WW I/stockpiled WW II |
| ω -Chloroacetophenone | CAP (CN) | Stockpiled WW II/civilian use |
| <i>o</i> -Dianisidine chlorosulphonate | | Minor sternutator WW I |
| Diphenylchloroarsine | DA | Sternutator WW I/stockpiled WW II |
| Diphenylcyanoarsine | DC | Sternutator WW I/stockpiled and used (China) WW II |
| 10-Chloro-5,10-dihydrophenarsazine | Adamsite (DM) | Sternutator stockpiled WW II |
| Phenyldibromoarsine | | Minor agent WW I |
| <i>N</i> -(4-hydroxy-3-methoxybenzyl)-8-methylnon- trans-6-enamide | Capsaicin | Minor WW I agent/civilian use |
| 2-Chlorobenzalmalononitrile | CS | Post WW II irritant, use in Vietnam War/civilian use |
| Dichloroformoxime | Phosgene oxime (CX) | Nettle agent stockpiled WW II |
| Non-irritating incapacitants | | |
| 3-Quinuclidinyl benzilate | BZ | Post WW II psychochemical |
| Choking agents (lung-damaging agents) | | |
| Chlorine | Cl | Major agent WW I |
| Bromine | | Minor agent WW I |
| Methyl chlorosulphonate | | Minor agent WW I |
| Ethyl chlorosulphonate | | Minor agent WW I |
| Phenylcarbylamine chloride | | Minor agent WW I |
| Bis(chloromethyl)ether | | Minor agent WW I |
| Bis(bromomethyl)ether | | Minor agent WW I |
| Trichloronitromethane | Chloropicrin (PS) | Major agent WW I, WW II stockpiled as lachrymator |
| Perchloromethyl mercaptan | | Minor agent WW I |
| Thiocarbonylchloride | Thiophosgene | Minor agent WW I |
| Carbonyl chloride | Phosgene (CG) | Major agent WW I, heavily stockpiled WW II |
| Trichloromethyl chloroformate | Diphosgene (DP) | Major agent WW I, stockpiled WW II |
| Hexachlorodimethyl oxalate | Thiophosgene | Post WW I developmental agent |
| Cadmium oxide | | Developmental WW II agent |
| Blood agents | | |
| Hydrogen sulfide | | Minor blood agent WW I |
| Methyl cyanofomate | | Minor blood agent WW I |
| Ethyl cyanofomate | | Minor blood agent WW I |
| Cyanogen bromide | | Minor blood agent WW I |
| Cyanogen chloride | CK | Minor blood agent WW I, stockpiled WW II |
| Hydrogen cyanide | Prussic acid (AC) | WW I agent, stockpiled WW II |
| Arsine | SA | Developmental WW II agent |

Table 3 (Continued)

| Chemical name | Common name/US code | Remarks ^a |
|--|--|--|
| Vesicants | | |
| Dimethyl sulphate | | Minor WW I agent |
| Phenyldichloroarsine | PD | WW I agent, stockpiled WW II as sulphur mustard additive |
| Methyldichloroarsine | MD | WW I agent |
| Ethyldichloroarsine | ED | WW I agent |
| Ethyl dibromoarsine | | Minor WW I agent |
| 2-Chlorovinyl dichloroarsine | Lewisite (L) | Stockpiled WW II, used in China mixed with sulphur mustard |
| Bis(2-chloroethyl)sulphide | Mustard gas, Yperite (H), distilled (HD) | Major WW I agent, heavily stockpiled WW II, several times allegedly used later |
| 1,2-Bis(2-chloroethylthio)ethane | Sesquimustard (Q) | Developmental WW II agent, most potent vesicant known |
| Bis(2-chloroethylthioethyl)ether | T | Stockpiled WW II as sulphur mustard additive |
| Bis(2-chloroethyl)ethylamine | HN-1 | Stockpiled WW II (minor) |
| Bis(2-chloroethyl)methylamine | HN-2 | Stockpiled WW II (minor) |
| Tris-(2-chloroethyl)amine | Nitrogen mustard (HN-3) | Stockpiled WW II |
| Nerve agents | | |
| Ethyl <i>N,N</i> -dimethylphosphoramidocyanidate | Tabun (GA) | Large scale manufacture WW II, use Iraq – Iran war |
| <i>iso</i> -Propyl methylphosphono-fluoridate | Sarin (GB) | Heavily stockpiled after WW II, use Iraq – Iran war |
| Cyclohexyl methylphosphono-fluoridate | Cyclosarin (GF) | Stockpiled and used by Iraq (Iraq-Iran War) |
| 1,2,2-Trimethylpropyl methylphosphonofluoridate | Soman (GD) | Stockpiled USSR after WW II |
| Ethyl <i>S</i> -2-diisopropylaminoethyl methylphosphonothioate | VX | Heavily stockpiled after WW II |
| Antiplant agents | | |
| 2,4-Dichlorophenoxyacetic acid | 2,4-D | Use in Vietnam War |
| 2,4,5-Trichlorophenoxyacetic acid | 2,4,5-T | Use in Vietnam War |
| 4-Amino-3,5,6-trichloropicolinic acid | Picloram | Use in Vietnam War |
| Dimethylarsinic acid | Cacodylic acid | Use in Vietnam War |

Modified from Robinson et al. (1973).

^a Major or minor agent relates to the amount used and duration of use.

1983–1988—Iraq–Iran war: use of sulphur mustard, tabun and sarin by Iraq Forces (Smart, 1997, Newmark, 2004).

1984—The Rajneeshi sect uses salmonella in order to manipulate US-elections (Torok et al., 1997).

1987–1988—Iraq campaign against the Kurds: use of sulphur mustard and sarin by Iraq Forces (Halabdjia Massacre 1988) (CNS, 2001).

1990–1995—Aum Shinrikyo terrorist attacks: the sect attempts fails to disseminate botulin toxins and anthrax spores (Carus, 1998).

1994—Aum Shinrikyo terrorist attack in Matsumoto: use of sarin (Tu, 1996).

1995—Aum Shinrikyo terrorist Attack in Tokyo: use of sarin (Tu, 1996).

2001—Anthrax letters, USA: distribution of letters that had been contaminated with anthrax spores (Ashraf, 2002).

October 23, 2002—Use of fentanyl analogues against rebels: assault made by Russian Special Forces in order to free hostages kept in a music-theatre in Moscow.

4. Development of chemical and biological warfare agents

4.1. Chemical warfare agents

After the German military forces had first used chlorine during WW I, many nations started intensive chemical warfare-programs for retaliation purposes. These efforts did not cease after the War but were even intensified during WW II. After WW II research mainly focused on nerve agents. After intensive testing, sarin and VX became standardized agents in the USA, where most of

the information comes from. But sulphur mustard and analogues were still kept in store.

4.2. Nerve agents

Nerve agents are organic phosphorus compounds (OP), i.e. esters of phosphonic or phosphoric acid as are some insecticides, flame retardants, plasticizers, softeners, emulsifiers and lubricating oil additives. The synthesis of the highly toxic OP tetraethylpyrophosphate (TEPP) had already been reported in the mid-19th century in the laboratory of De Clermont in France and later has been successfully repeated several times by other chemists. However, the high toxicity of this agent as well as of other compounds of this chemical group had not been recognized until the 1930s when Lange and Krüger described effects, which they noticed during synthesis of some OP with the P–F bond (Holmstedt, 1963).

In 1934, a project on synthetic insecticides was started at I.G. Farbenindustrie (Germany) by Otto Bayer who assigned all further research to the chemist Gerhard Schrader. In 1936, his interest turned to OP compounds. In March 1937, he patented the general formula of all contact insecticides of this type. His systematic work with OP insecticides led to the synthesis of more than 2000 compounds, among them the highly toxic ethyl-*N,N*-dimethylphosphor-amidocyanidate (tabun) in 1936 (December 12; Robinson and Leitenberg, 1971) and isopropyl methylphosphonofluoridate (sarin) in 1937. Since 1935, an official decree required for all inventions of possible military significance to be reported to the German Ministry of War. In 1937, samples of tabun and sarin were sent to the CW section of the German Army Weapons Office (Wa Prüf 9) where their value for military purposes had immediately been recognized and hence all patent applications concerning these agents were declared secret (Holmstedt, 1963; Robinson and Leitenberg, 1971). About 200 compounds were categorized as secret agents, including the well known TEPP, but out of these only tabun, sarin and soman reached practical relevance as CW agents (soman after WW II).

While in 1939, a pilot plant was set up in Munsterlager/Heidkrug, the full scale industrial production of tabun did not start until January 1940 at Dühernfurt, Oder. The first lot was produced in May 1943. The production of sarin was hampered by difficulties caused by the extremely corrosive hydrofluoric acid, which was required for the manufacturing process. The construction of a large-scale production factory at Falkenhagen was started in 1943 but was not finished until after the war. Pinacolyl methylphosphonofluoridate (soman) was syn-

thesized in 1944 by the Nobel laureate Dr. Richard Kuhn. Until the end of the war, about 10,000–12,000 tonnes of tabun, 600 tonnes of sarin and only laboratory-scale amounts of soman were produced (Holmstedt, 1963; Robinson and Leitenberg, 1971).

Research on OP compounds during WW II was also performed in English laboratories and later in US laboratories and was mainly focussing on diisopropylfluorophosphate (DFP) as one of the most prominent agents. It was only after WW II, when the German research project became known, that nerve agents gained military significance and intensive research was also started in the USA, in England, France and the Soviet Union.

Although their mechanism of action, i.e. cholinesterase inhibition, was discovered during WW II by German, English and US scientists, the data were published only after the War (Holmstedt, 1963). The importance of atropine as an antidote was recognized in German laboratories and first came to use in victims of accidents during the development and production in the course of WW II.

After WW II, sarin was adopted by the USA and the USSR and was stockpiled in large amounts of several thousands of tonnes. Furthermore, the Soviet Union also stockpiled large quantities of soman (Robinson and Leitenberg, 1971). In addition to military laboratories insecticide manufacturers also became very interested in organophosphorus compounds. In the early and mid 1950s, at least three laboratories investigated the class of highly toxic organophosphate esters of various 2-aminoethanethiols, with first results being published by R. Ghosh and J.F. Newman from ICI Ltd. Studies were also performed by Schraders laboratory at Farbenfabriken Bayer and by Tammelin in the Swedish chemical warfare laboratories. In 1955, a team from the I.M. Sechenov Institute, Leningrad also started to look on this class of compounds (Robinson and Leitenberg, 1971). Shortly after their discovery at the ICI their existence had been reported to the British CW Establishment in Porton Down. As a result combined investigational efforts were made by British and US Laboratories resulting in the development of the new V-class nerve agents. VX was chosen as the most promising substance and full scale production commenced in 1961 in the USA. Until nowadays, VX appears to be the most effective chemical warfare agent ever produced. The lethal dose for humans is estimated to be about 0.3 mg/person after inhalational and 5 mg/person after dermal exposure. Chemical variants were also produced in the Soviet Union and in China. Sarin and VX became the standard nerve agents in the USA.

In the 1950s, the Binary Weapons Program was started in the USA. According to this binary concept, two less toxic reactants are mixed together in the weapon after it has been fired or dropped, thereby creating the actual nerve agent. This allows for safer handling of ammunition. In the USA, binary projectiles for sarin and VX were developed (Smart, 1997).

4.3. Vesicant agents

4.3.1. Sulphur mustard

While investigating the reaction of sulphur chloride with ethylene in 1822 Cesar Despretz discovered a strange smelling liquid, which reminded him of horse radish or mustard, without recognizing its toxic properties. In 1860, 2,2-dichlorodiethylsulfide, also known as sulphur mustard (SM), was synthesized by Guthrie in the United Kingdom and Niemann in Germany (Guthrie, 1860; Niemann, 1860). The production of the purified compound was first reported by Meyer (1886).

While the toxic potential of most other chemical agents employed in WW I had been recognized during their industrial use (e.g. chlorine and phosgene), SM had explicitly been developed as a chemical warfare agent. Its first use on the battlefield was conducted by German Forces on July 12, 1917, and was based on the work of Lommel and Steinkopf, whose initials gave this substance its name: Lost. As from 1919, the latter chemist became head of the organic chemistry department at the university of Dresden. Due to the German practice of marking SM containing shells with a yellow cross the agent was also named Yellow Cross. It was the first agent intended to injure masked soldiers by causing skin lesions and cutaneous uptake. Indeed, the number of chemically injured soldiers increased rapidly. In contrast to other agents and weapons, the lethality was comparatively low (about 2%) (Robinson and Leitenberg, 1971) although the number of injured with late effects was high (Szinicz and Baskin, 1999).

The US (NATO) code for SM is H, and originates from the English slang word for Germans, i.e. Huns. Later on, mainly the distilled preparation had been used and therefore was called HD. Being the major chemical agent during WW II, SM was produced and stockpiled by many countries and probably still is the most distributed chemical warfare agent in the world. During WW II, the analogue bis-(2-chloroethylthioethyl)ether was developed, which turned out to be more persistent and three times more toxic than the parent compound. Being coded HT, this agent was fielded in the USA as a chemical mixture with 60% SM. It remained a part of

US stocks and is or will be destroyed with other agents due to OPCW regulations.

4.3.2. Nitrogen mustard

After WW I, considerable efforts were made to identify new analogues of known chemical warfare agents with higher efficacy. Nitrogen analogues to SM were investigated. The most prominent ones were tris-(2-chloroethyl)amine, methyl- and ethyl-bis-(2-chloroethyl)amine which received the US-codes HN 3, HN 2 and HN 1, respectively. During WW II, the USA produced about 100 tonnes of HN 1 and Germany roughly 2000 tonnes of HN 3 (Robinson and Leitenberg, 1971). Observations that SM and nitrogen mustards have similar biological effects as ionising radiation (radiomimetic effect) led to the use of nitrogen mustards in the treatment of leukaemia. More intensive research during WW II led to the development of less cytotoxic analogues providing the basis for further progresses in the field of cytostatic therapy of malignant diseases (Ross, 1962; Calabresi et al., 1985).

4.3.3. Arsenical vesicants

Shortly after research on SM had begun in Germany, organic arsenicals were being investigated also. German agents were ethyldichloroarsine, methyldichloroarsine and ethyldibromoarsine, which were first used on the battlefield in March and for the last time in September 1918. At first, shells containing these agents were marked with a Yellow Cross according to their vesicant-like properties, but when their capacity for skin damage (especially for ethyldichloroarsine) was recognized to be low, their marking was changed to a Green Cross, symbolizing their primarily lethal respiratory effects. During its developing phase 2-chlorovinyl-dichloroarsine was rejected. This compound was simultaneously investigated in the USA, where it became the mean organoarsenical vesicant. It was discovered by Captain W.L. Lewis at the Catholic University, Washington, DC in the spring of 1918 and received the code L. A ship with lewisite had already been on its way to Europe in November 1918, but because of the early end of WW I could not be delivered to the battlefield in time. US investigations during WW II revealed lewisite vapors to be inferior to SM in producing skin and eye lesions. Although lewisite liquid by cutaneous route proved to be systemically more toxic, SM-induced lesions turned out to be more severe. SM also proved to be more persistent and superior in penetrating clothing materials. Therefore, it lost its priority in US stockpiles. The USSR and Japan used lewisite as an antifreeze additive for SM (Robinson and Leitenberg, 1971). Large

stockpiles of thousands of tons of lewisite were hence declared by Russia to the OPCW, which have to be destroyed.

4.4. Lung-damaging agents (choking agents)

4.4.1. Chlorine

After the battle of the Marne, the progression of German forces was stopped and the mobility of the belligerents changed to trench warfare. German stockpiles of high explosives were almost exhausted and the sea-blockade by the allies further deprived the Germans of raw materials for manufacturing explosives (mainly nitrates from Chile). On the battlefield non-explosive weapons were already being used (irritants). Under these circumstances, the German Supreme Command held a General Staff conference with leading industrial chemists of the time in order to solve the ammunition crisis. Two strategies were elaborated. The first strategy included a large-scale use of lethal chemicals on the battlefield. The second was to accelerate the development of the Haber process, which had already been established at laboratory scale, in order to synthesize ammonia from air for the production of high explosives. In both cases, the IG Farben company and the leading chemist of that time, Prof. Haber, were of central importance. Haber decided to employ chlorine in cylinders. On April 22, 1914, 498 tonnes of chlorine were discharged from 20,730 cylinders at Ypres. The German Supreme Command judged the “field experiment” as a success, although not being fully utilised from the tactical point of view. The attack indeed offered no tactical advantages, but on the contrary resulted in massive efforts on the part of the allies to respond with equal means. This event marked the very beginning of large-scale chemical warfare, i.e. the use of chemical weapons of mass destruction in the field (Robinson and Leitenberg, 1971). Soon, the belligerents moved on to replace chlorine by more effective agents, e.g. phosgene, diphosgene and chloropicrin.

4.4.2. Phosgene

Phosgene (gr. phos: light; genes: born) (carbonyl chloride), was discovered in 1812 by J. Davy, who investigated the effect of sunlight on a mixture of carbon monoxide and chlorine. This compound turned out to be almost 10 times more toxic than chlorine, even if the observed effects, e.g. a delayed toxic pneumonitis (so-called toxic lung oedema) were similar to those induced by chlorine. Nowadays, phosgene still is an important industrial chemical as it is necessary for the production of numerous chemicals and pharmaceuticals. During WW

I, it had first been used by Germany in December 1915, and later on by all other belligerents who usually released the agent from cylinders and shells. Later also the similarly acting diphosgene (trichloromethyl chloroformate), had been introduced, and had first been used by Germany in May 1915. Phosgene and phosgene/chlorine mixtures generated the highest mortality rates in comparison to other chemical agents used during WW I. It remained the standard non-persistent chemical warfare agents during WW II, and was produced and stockpiled in many countries (Robinson and Leitenberg, 1971).

4.5. Blood agents

4.5.1. Cyanides

Hydrocyanic (prussic) acid had been known since ancient times. Liquid hydrocyanic acid was first synthesized by Scheele in 1782. Berthollet identified the elements carbon, nitrogen and hydrogen as chemical constituents. Gay-Lussac was the first researcher, who succeeded in liquefying hydrocyanic gas in 1811 and reported its chemical composition in 1815 (Foerst, 1962). Theoretically, this substance appeared to be an ideal weapon because of its high toxicity, fast action, high volatility, i.e. high air concentration as well as its simple manufacturing process. Indeed, during WW I French forces produced high amounts of HCN. On the battlefield, however, the success was low. When using low payload projectiles, it turned out to be almost impossible to achieve lethal concentrations of HCN under field conditions, since the specific weight of its vapour is lower, compared to air, and also because of its tendency to rapidly evaporate. Therefore, other agents were preferred. During WW II cyanide preparations (Zyklon B; silica adsorbed cyanide) were used for homicide in German concentration camps.

Investigations in the USA and Japan during the 1930s have shown, that vaporization of high payloads of HCN caused enough of a cooling effect to increase persistence of the HCN cloud on the ground until being warmed up again (pancake effect). While the Japanese had introduced 50 kg bombs during WW II, the Americans found out that 500 kg payloads were the optimum charge.

Nevertheless, in the course of WW II the first nerve agents were being developed which showed much higher toxicity and good skin penetrating properties, thus rendering cyanide a less attractive chemical agent. On the other hand, cyanides still remain an alternative for terrorist attacks and in that way still pose a serious risk.

Cyanogen chloride (CK) was used in only small amounts by the French during WW I. It was re-examined by the US Army after the war and stockpiled during WW

II since it turned out to be a potential mask-breaker for Japanese masks under humid (tropic) conditions. With the appearance of nerve agents it became obsolete.

4.6. Incapacitating psychochemical agents

This class of chemical agents is intended to cause casualties by incapacitating exposed individuals due to its psychotropic actions without causing permanent harm or death. The only compound of this class, which is known to have been developed and tested for field-use and which has also been produced in substantial amounts in the USA after WW II was 3-quinuclidinyl benzilate. Being a potent antimuscarinic, this substance obtained the code BZ. Presumably because of the unpredictable nature of its effects, thus being of limited value for military use, and also because of its high manufacturing costs, the interest in this compound faded until further research was stopped.

4.7. Irritants (*Lacrimators, Sternutators*)

Before lethal agents like chlorine and phosgene appeared on the battlefield during WW I, several primarily irritating agents (harassing agents) were used (Table 3). The first field-use of an irritant took place in August 1914 when French Forces used ethylbromoacetate. This employment was based on good experiences of the French police with rifle cartridges and hand grenades filled with this chemical before WW I.

Consisting of a high explosive and *o*-dianisidine chlorosulphonate (Niespulver—sneezing agent), the so-called Ni-Schrapnell was first tested by the Germans in October 1914 at Neuve-Chapelle, according to recommendations of Prof. Nernst. However, the test failed and afterwards the agent was not used any more. Several thousands of irritants (harassing agents) have been tested and used on the battlefield by different belligerents during WW I (Table 3) (Robinson and Leitenberg, 1971).

The most extensively used irritant during WW I was bromoacetone. At the end of WW I very potent irritating agents were developed by the French (*a*-bromobenzyl cyanide; CA) and the Americans (*a*-chloroacetophenone; CN), the latter still being used and stockpiled for riot-control and civil protection (Chemical Mace). In 1917, the Germans introduced a new class of irritants (Blue Cross agents; diphenylchloroarsine; DA and diphenylcyanoarsine; DC). Because of its easier manufacturing properties, the British and Italians preferred 10-chloro-5,10-dihydrophenarsazine (DM). In the USA, the substance has been named Adamsite accord-

ing to its discovery by a team, which had been working under Major Roger Adams early in 1918. At the same time, a British team also discovered the compound yet both parties were unaware of an already existing German patent from 1914, which described its synthesis. These arsenicals were also produced by many countries shortly before and during WW II (Robinson and Leitenberg, 1971).

After WW I, in numerous countries CN became the standard harassing agent for military use and for civil riot-control even if partly being replaced by 2-chlorobenzalmalonodinitrile (CS) after WW II.

CS was discovered by two US chemists, R.B. Corson and R.W. Stockton in 1928 and was introduced on behalf of British efforts to replace CN in the mid 1950s. The code reflects the initials of the discoverers' names. A large-scale military use of the agent was conducted by US Forces in Indochina (Viet-Nam). During that time either CS with a pyrotechnic matrix, micronised CS with silica (CS 1) or silanised micronised CS powder (CS 2) were being used.

4.8. Biological agents

Although some programs for the development of biological warfare agents were already performed during WW I, major programs on weaponized biological agents were only started shortly before or during WW II. More detailed information is only available about the programs of Japan, the USA, Canada, the United Kingdom and Germany (Robinson and Leitenberg, 1971). A summary of agents, which reached field-testing is given below (see also Table 4).

After WW II, the newly discovered technology of lyophilization became an important input for the development of biological warfare agents. Not only human pathogens but also antiplant pathogens were investigated. The Iraq also produced biological agents in al-Hakam until 1991. These efforts did not become generally public until 1995, when it could be demonstrated that botulinal toxins, anthrax and aflatoxin had been produced.

In modern times, an actual use of biological warfare agents in military conflicts has never been confirmed. The most prominent example of terrorists using biological warfare agents has been the distribution of anthrax letters in October 2001 in the USA.

In November 1969, US President Richard Nixon renounced the use of biological weapons and gave the order to restrict research efforts to merely defensive aspects. Between 1971 and 1973, all remaining US biological weapons were destroyed (Smart, 1997).

Table 4
Potential biological warfare agents

| Disease | Causative agent (Code) | Remarks ^a |
|-------------------------------------|---|--|
| Antipersonnel agents | | |
| Toxins | | |
| Botulism | Botulinal toxin A (X) | Stockpiled after WW II |
| Castor bean | Ricin (W) | Developmental toxin after WW II |
| Paralytic shellfish poisoning | Dinoflagellates as <i>Gonyaulax catanella</i> ; Saxitoxin (TZ) | Small stockpile after WW II |
| Viruses | | |
| Yellow fever | | Standardized agent; mosquito as vector |
| Venezuelan equine encephalomyelitis | VEE Virus | Standardized agent |
| Rickettsiae | | |
| Q fever | <i>Coxiella burnetii</i> | Standardized agent |
| Bacteria | | |
| Plague | <i>Yersinia pestis</i> | Allegedly used by Japanese in China |
| Anthrax | <i>Bacillus anthracis</i> | Standardized agent |
| Cholera | <i>Vibrio cholerae</i> | Allegedly used by Japanese in China |
| Tularemia | <i>Francisella tularensis</i> | Standardized agent |
| Brucellosis | <i>Brucella</i> spp. | Standardized agent |
| Antiplant agents | | |
| Rice blast | <i>Pyricularia oryzae</i> | Standardized agent |
| Wheat stem rust | <i>Puccinia</i> spp. | Standardized agent |

^a Standardized, developed to field use, Modified from Robinson et al. (1973), Smart (1997).

4.9. Toxins

Capsaicin, the pungent principle of cayenne pepper and paprika was being tested by the USA during WW I and II with regard to its usefulness in warfare. During the 1950s it has also been tested by the British as a possible substitute for CN as a riot-control agent. Though never reaching military importance this agent still is being used for riot-control by police forces in several countries and furthermore is being manufactured for individual protection (self-protection) against criminals and dogs.

Ricin, the toxic ingredient of castor beans, had been identified as hazardous by-product of castor oil production since the 19th century. During WW I, it was intensively tested by the USA, Canada, Great Britain and France. Field tests were performed by the USA during WW II.

Botulinal toxins, the most toxic compounds ever known are formed by *Clostridium botulinum*. Since the 1930s, these toxins have been tested especially during and after WW II by the USA, Canada and Great Britain. Canada developed a large-scale production method for botulinal toxins during WW II in cooperation with the USA and the United Kingdom. It should also be noted that botulinal toxins are produced for use in medicine.

Saxitoxin first became known when intoxications occurred after consuming poisonous shellfish. Paralytic shellfish poisoning has been known as a clinical entity

since the 19th century. The toxin first has been isolated during WW II in the USA within the scope of an US BW program. The fact that saxitoxin is produced by dinoflagellates like *Gonyaulax catanella* did not become known until the 1960s.

Staphylococcal enterotoxin, produced by *Staphylococcus* bacteria is the active principle of food poisoning. The most extensively studied form is the staphylococcal enterotoxin B (SEB), which is produced in large and easily isolatable yields by *Staphylococcus aureus*. Although being not primarily lethal, it still proved to be very stable also causing severe and debilitating symptoms.

4.10. Microorganisms

4.10.1. Gastrointestinal bacteria

In the scope of the Japanese biological warfare program (1934/1935–1945) in Manchuria (Pingfan near Harbin) several gastrointestinal pathogens were investigated as possibly causative agents of typhoid fever, dysentery and cholera.

4.10.2. *Bacillus anthracis* (anthrax)

Anthrax germs were field tested within the Japanese biological warfare-program during WW II. While agent-distribution via the so-called Uji bomb (see plague) was accomplished by the formation of an airborne bacterial cloud, the Ha bomb was designed to disseminate

anthrax-contaminated shrapnel, which had been set free by explosion. Anthrax spores were also field tested by the British in small aircraft bombs and cannon shells on Gruinard Island at the northwest coast of Scotland in 1941 and 1942. The island remained contaminated for more than 50 years due to the high stability of the spores in soil.

4.10.3. *Pasteurella pestis* (plague)

In the course of their WW II-program, Japanese scientists also investigated vectors for the dissemination of BW (i.e. plague-infected flea). Field trials were performed in 1941 and 1944 (Robinson and Leitenberg, 1971). For dissemination of *Pasteurella pestis* likewise the so-called Uji bomb was tested, which consisted of a frangible porcelain casing to be scattered by a small powder charge.

5. Protective measures against chemical and biological agents

5.1. Respirator

Until July 1917 (first use of SM), all that had been necessary in order to protect troops against chemical agents was to provide them with respirators containing filters for removal of airborne contaminants before inhaled air could reach their lungs. The first proposal concerning the use of respirators is reported to have been made by Leonardo da Vinci in the 15th century (Smart, 1997). This preliminary archetype consisted of a fine cloth dipped in water for defence against a sulfide of arsenic and verdigris powder, the assumingly employed toxic weapon. During the second half of the 19th century different respirators were being developed, some of them including an activated charcoal filter and eye-protection devices. Therefore, it is all the more astonishing, that German troops had only been equipped with a very primitive respirator (i.e. a cotton cloth, which had to be soaked with neutralizing chemicals to cover mouth and nose), when for the first time employing a lethal lung-damaging agent (chlorine) as a weapon of mass destruction. This fact seems even more peculiar, as the agent had been released from cylinders, imposing a high risk of accidental exposure of own troops due to turning winds. The allied forces were surprised by this first attack and hence the first respirators (for the soldiers) could only be introduced with some delay. However, they were constructed after the same principle, as they consisted of a cotton cloth soaked mostly with bicarbonate or thiosulphate solutions.

Towards the end of 1915, German forces introduced a respirator, which included an eye-protection device. In addition, a drum, which contained the sorbent could be screwed to the mouthpiece. In the winter of 1915/1916, the British forces also introduced an eye-protecting respirator consisting of a large box, which contained the sorbent in a satchel that could be slung over the back. This device proved to have a much greater absorption-capacity, compared to the German respirator. While at that time the main disadvantage of the German respirator had been its low adsorptive capacity as well as some problems concerning the fitting of the mask during the battle (due to the weight of the drum), the construction principles have been followed by most nations until present times.

The development of adequate filter units had been a race between chemists, which were developing new agents with new properties, and facilities, which were constructing new protective filters. In July 1917, the first compound of a new class of irritating agents, the diphenylchlorarsine had been used on the battlefield by German forces. Being solids at room temperature, these agents were liberated by incineration and after condensing to a very fine aerosol could pass protective filters of that time. Moreover, their toxic effects, i.e. irritation and vomiting were protracted and forced the exposed individuals to remove their respirator. Therefore, these agents were also called mask breakers and the shells were being marked by a blue cross. At that time, British masks had already been equipped with an aerosol filter (with other belligerents soon following the British standard), which limited the further use of this class of agents. Nevertheless, at the same time the vesicant SM had been introduced, which raised the problem that mere eye and airway protection was not sufficient any more. Among additional protective measures, which had been tested at the end of WW I were protective suits, barrier creams and skin decontaminants (see there).

After WW I and during WW II the respirators were improved with regard to their body-material (better fit, communication and sight) as well as their filter components. Even at present, the basic principle of the filter consists of activated charcoal and an aerosol component. Many filters also contain various combinations of copper, silver, chromium and pyridine or picoline impregnants for protection against HCN and cyanogen chloride.

5.2. Skin protection

Impermeable oilcloth came into use shortly after the introduction of SM. However, it had been too heavy,

cumbersome and uncomfortable and therefore its use has been limited to special troops (e.g. gun crews), for which keeping in action had been essential. The second measure that had been used in parallel, were barrier creams. This protective procedure turned out to be of limited value since SM was surprisingly penetrative and troops were not able to apply the cream continuously. Best effects were observed when the cream was applied shortly before an assault.

One strategy of improving protective clothing after WWI and during and shortly after WW II was to impregnate ordinary combat-clothing. Indeed, this measure was sufficiently effective for protection against SM but completely insufficient for nerve agents. The second strategy, which turned out to be more effective consisted of a protective cloth that had been impregnated with activated charcoal. This technique had first been developed by the British and thereafter had also been introduced by many other armies. As supplementary measure or even as an alternative, impermeable overgarments were being developed to be worn over the normal battle-dress. Furthermore, impermeable capes have been used to protect these rain-sensitive charcoal-impregnated suits. The protective suit was completed by impermeable boots and gloves (besides of the respirator).

Even nowadays complete protection can only be accomplished when using an impermeable suit. Although by the time this type of protection became much more comfortable and light-weight, the inability to warrant moisture transport thereby comprising the danger of heat-strokes in warmer environments or under increased physical activity limits its usefulness.

5.3. *Detection*

Until the appearance of nerve agents, early warning equipment was more important for demasking than for masking as the agents had their own characteristic odour or were irritating. Nerve agents nearly do not smell even at lethal concentrations. Therefore, almost all armies have developed early warning devices (indicator paper, portable and more heavy detection systems), which improved by the time due to technological advances. In general, portable light-weight detection equipment is not very specific, and the risk of false-positive alarms is high.

5.4. *Decontamination*

After the French had begun to use SM, German soldiers received boxes with bleaching powder or permanganate for decontamination. However, success was

scarce, because frequently contaminations were not noticed in time. Furthermore, carrying along the box also put an additional burden on the soldiers.

Nevertheless, bleaching powders in various preparations, mostly combined with adsorbing material, e.g. magnesium oxide, or adsorbing material alone, e.g. Fullers earth, still provide the basis for skin decontaminants in most armies. Most of the time chemical reactions are taking place too slowly, especially at lower temperatures or in absence of a solvent, thus necessitating an adsorbent to stop the penetration into the skin in time. However, dilution of the agent would produce the same effect.

Powders are not appropriate for decontamination of mucous membranes (eyes) and wounds as bleaching powder can cause serious damages in the above-mentioned tissues. Therefore, all preparations, which contain bleaching powder are not appropriate for decontamination of the face. At present, skin decontaminants, which are lacking dangerous effects to mucous membranes and wounds are being developed. These are based on enzymes or specific chemicals like oximes for rapid nerve agent destruction. All these measures are primarily designed for decontamination of exposed skin areas. For whole-body decontamination even at present the application of copious amounts of water is the decontamination method of choice. Corresponding equipment for decontamination is being introduced in most armies.

5.5. *Medical countermeasures*

Before the era of nerve agents therapeutic strategies for the treatment of injuries caused by chemical agents had merely been restricted to supportive measures. In addition, early sensory warning of exposed individuals (by specific odours or irritation in combination with the wearing of respirators), a good anti-gas discipline and effective decontaminants warranted sufficient protection. After the introduction of nerve agents, the uptake of rapidly incapacitating or even lethal doses became a regular event, which prevented the victims from carrying out appropriate self-protection measures in time. This development called for adequate countermeasures. An atropine syrette for self injection was introduced in the US Army in 1950. This device was replaced by an autoinjector with a spring-driven needle in 1959 (Smart, 1997). Self and buddy aid with autoinjectors for rapid on the spot application of antidotes (later a combination of atropine and an oxime was favoured), has been advanced and nowadays has become the standard in most armies. Indeed, in combination with effective respirators

and protective suits this countermeasure cannot reduce the number of casualties but can help to save life.

6. International control of chemical and biological weapons

1675—Strasbourg Treaty: Germany and France agree on banning the use of poisons in warfare, i.e. the contamination of water supplies, food or weapons.

1874—Brussels Conference: The “International Declaration Concerning the Laws and Customs of War” which includes a prohibition of poison or poisoned arms is signed.

1899—First Hague Conference: Banning of the use of poisons. “The contracting powers agree to abstain from the use of projectiles the sole object of which is the diffusion of asphyxiating gases”.

1907—Second Hague Conference: The ban of poisons by the First Conference is retained.

1922—Washington Conference: Delegates from the USA, France, the United Kingdom, Italy and Japan decide to ban the use of suffocating, poisonous and other gases. France refused to ratify, and the treaty was never implemented.

1925—Geneva Protocol: Protocol for the “Prohibition of the Use in War of Asphyxiating, Poisonous or Other Gases, and of Bacteriological Methods of Warfare”. Signed at Geneva on June 17, 1925 by 30 nations.

1972—Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and their Destruction (BTCW): Signed in London, Moscow and Washington on April 10, 1972, entering into force as from March 26, 1975.

April 29, 1997—Chemical Weapons Convention (CWC) entry into force: Ban of the development, production, acquisition, stockpiling and transfer (direct or indirect), of chemical weapons. The use of chemical weapons, the engagement in any military preparations aimed at using chemical weapons and the assistance, encouragement or induction of such activities is prohibited by the convention. Each participating/signing nation undertakes measures to destroy their (own) chemical weapons and production facilities and commits to not using riot-control agents as a method of warfare. For control of compliance with the CWC, the Organisation for Prohibition of Chemical Weapons (OPCW) in The Hague was installed.

The CWC was opened for signature in Paris, on January 13, 1993. At present the number of ratifications and accessions is 162 (6 September 2004).

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