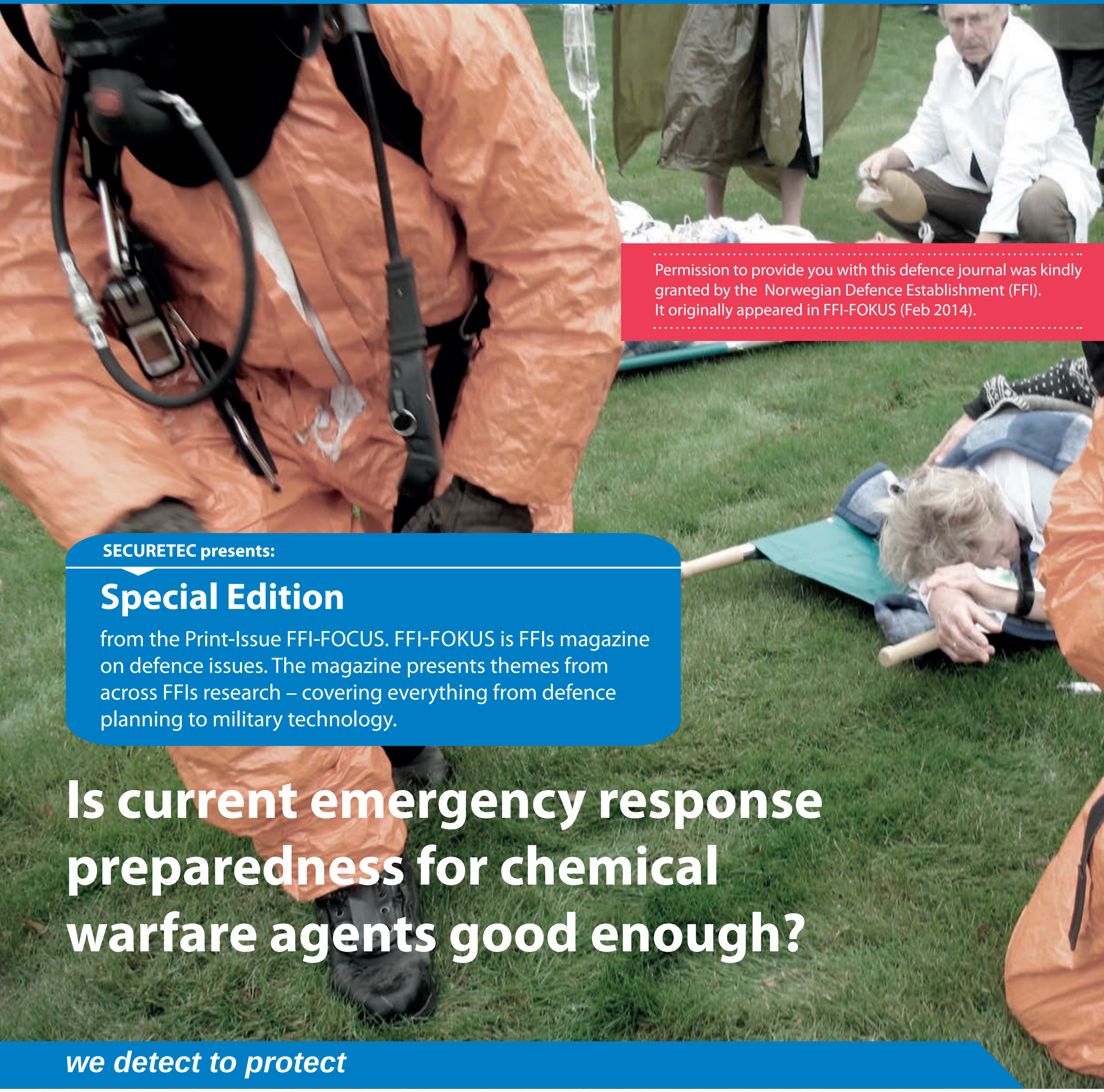
DIAGNOSIS OF NERVE GAS POISONING



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Is current emergency response preparedness for chemical warfare agents good enough?

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Use of chemical warfare agents – improvements needed for emergency medical preparedness

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Chemical warfare agents constitute a real threat both to Norwegian soldiers in foreign countries and to targets in Norway. Deployment in Syria is a disturbing reminder. Is Norway sufficiently prepared?

In the course of 2013, a number of articles appeared in the news claiming that chemical warfare agents may have been used against civilians in multiple attacks at various sites in Syria during the ongoing civil war. The UN Secretary General, with the support from the UN Security Council, has decided to establish an inspection group to ascertain whether these claims were accurate. This group was appointed on 21 March 2013 and was a collaboration between the World Health Organization (WHO) and the Organization for the Prohibition of Chemical Weapons (OPCW). However, it wasn't until after the attacks against civilians on 21 August 2013 and after strong pressure from the USA, United Kingdom and France, amongst others, that the inspectors obtained permission from the Syrian authorities to conduct the necessary inspections at different locations around Damascus. These attacks resulted in very many people, including children, being injured and killed. The civilian population and health services were unprepared for the use of such weapons and the extent of injuries was therefore large. On 16 September 2013, unequivocal proof was obtained that the nerve gas sarin had been used, but the UN mandate did not extend to the identification of those responsible for the use of such weapons. This therefore has still to be established.

Terrorist attacks in Norway

Could such weapons be used in Norway? Are front-line services, such as hospitals, fire and rescue service, police and civil defence sufficiently prepared and trained to be able to handle situations where chemical warfare agents or highly toxic chemicals are deployed? Is the emergency response, including storage of the necessary equipment and drugs, adequate, even outside of the central parts of Oslo? Can the injured receive adequate treatment? To be able to reassure the population, the government should be able to acknowledge these issues.

In 2011, two terrorist attacks took place in Norway, one in Oslo and one in Buskerud, which resulted in a total of 69 dead and many injured. These attacks were carried out using conventional means. The Norwegian perpetrator has published a manifesto on the Internet which amongst other things discusses the effects that can be achieved through the use of various types of chemical warfare agents and other chemicals as terrorist weapons. International analysis of the manifesto in 2011 by the Federation of American Scientists, amongst others, concludes that there are technological challenges to the synthesis and efficient dissemination of such agents that are likely to exceed many terrorists' level of knowledge, including the Norwegian terrorist, but that this is a threat that should definitely be taken seriously. The report from the 22 July Commission concluded that the "vital elements of the authorities' emergency response and crisis management capability were not good enough".

On 23 August 2011, in a speech at the Norwegian Defence University College, Defence Minister, Grete Faremo, declared that WMDs pose a serious threat. This underlines the importance of ensuring that security is viewed with the utmost seriousness, even in Norway, and updates a review of all levels of emergency preparedness to such incidents.

‣ In 2012, an exercise was carried out at the hightox laboratory of the Norwegian Defence Research Establishment *[Forsvarets Forskningsinstitutt – FFI]*; the scenario was an accident involving nerve gas. Several of the emergency services took part. *Photo: FFI*

A Government White Paper on "Civil Protection" [Report no 29 to the Storting (2011-2012)] and a report on "Preparedness for Terrorism" [Report no 21 to the Storting (2012-2013)] have been drawn up on the basis of deficiencies in emergency preparedness in Norway. In these two white papers, the government sets out new key initiatives for civil protection and emergency preparedness and an overarching strategy for this work going forward.

What are chemical weapons?
Chemical weapons, together with biological and nuclear weapons, are defined as weapons of mass destruction due to their ability to kill and maim. Chemical weapons are defined in the two major disarmament agreements in this field; the Geneva Protocol of 1925 and the Chemical Weapons Convention which came into force in 1997. These weapons are defined as toxic chemicals, their precursors, munitions and components and devices used in connection with the use of such munitions. Toxic chemicals can be any chemical which causes death, temporary incapacitation or permanent harm to humans or animals or a range of special-purpose chemicals which are defined in Chemical Weapons Convention.

Standard chemical and biological weapons represent the extremes of a spectrum of current threat agents which includes the misuse of pharmaceuticals and insecticides, naturally occurring toxins, neurotransmitters in the nerve system of humans and animals and genetically modified biological threat agents (Figure 1). By using new chemical synthesis and production methods and biotechnological methods, more potent toxins and effective compounds, in addition to standard weapons, can be produced more easily, more cheaply and in greater quantities than in the past.

What are chemical warfare agents?
Chemical warfare agents are the toxic chemicals that are added to different types of weapons carriers, such as bombs, rockets, grenades, mines and small and large missiles, which together make up a chemical weapon. The most well-known of the standard chemical warfare agents are the nerve gases which are known for their extreme toxicity (Table 1). Nerve gases work by blocking the nerve impulse transfer, severely impairing, amongst other things, the function of the nerve cells in the brain and causing the muscles of the affected person to convulse powerfully. A few milligrams is enough to kill. Use of such weapons will not be detected immediately since nerve gases are invisible and odourless. However, the onset of symptoms of poisoning and death appear rapidly unless appropriate medical treatment is administered immediately. Nerve gases and mustard gas are liquid at normal room temperature. Their effect is most often achieved by vaporisation – hence the term "gas".

Blister agents, such as mustard gas, however, smell like mustard or garlic, and do not work as quickly as nerve gases, causing damage mainly to the lungs, eyes and skin. We remain unaware that we have been poisoned several hours after exposure to mustard gas when is it too late to prevent damage. In the event of severe poisoning, injuries may be so extensive that we do not survive such an exposure.

Psychochemical warfare agents were also developed in some countries after the Second World War. These are warfare agents which impair the ability to fight by affecting the nerve system and altering the victims' perception of reality. Tear gases, however, have very low toxicity and are safe when used according to instructions. These cause temporary stinging of, amongst other things, the eyes, nose and throat and are permitted for use in riot control but not as a method of warfare.

History
Chemical weapons were first used on a large scale in the First World War. Both Germany and the allies used chlorine, phosgene, mustard gas and tear gas-like substances. About 1.3 million people were injured and 100,000 people died of acute poisoning after use of these weapons. Half of those exposed and injured were Russians. In the period before the Second World War, chemical weapons were used in some bilateral conflicts, especially in Africa.

However, during the Second World War, despite the fact that Germany had developed nerve gases, chemical weapons were not used in Europe. In later times (1980s) it was proved that Iraq used chemical weapons against Iran and against the Kurds in northern Iraq. In addition, there have been numerous claims of the use of such weapons in international conflicts during the "cold war" but this has not been confirmed.

In Japan in 1994 and 1995, the sect Aum-Shinrikyo used nerve gas as a terrorist weapon. The most well-known attack was on the Tokyo underground system, where twelve people were killed and many injured. The reason that the number of dead and injured was low is the fact that terrorists do not have the technology available for the efficient dissemination of nerve gas.

International disarmament agreements
The 1925 Geneva Protocol imposed a ban on the use of chemical and biological weapons. The 1997 Chemical Weapons Convention is a very comprehensive disarmament agreement which also contains a comprehensive verification protocol which allows the ban on the development, production and storage of chemical weapons to be monitored at any time by the OPCW in The Hague in the Netherlands.

At the end of 2013, 190 countries have ratified the Chemical Weapons Convention after Syria agreed in September 2013 to hand over all its chemical weapons for destruction, but there are still some countries in the Middle East (Israel and Egypt), Asia (North Korea and Myanmar) and Africa (South Sudan and Angola) that have not ratified the Chemical Weapons Convention, and these countries are therefore not subject to international monitoring.

The Chemical Weapons Convention is therefore the most comprehensive and successful disarmament agreement ever established. Meetings are held each year at the UN in Geneva to seek to extend the monitoring programmes to biological weapons, so that compliance with the Biological Weapons Convention, which came into force in 1975, is verifiable, although this has proved very difficult to implement.

The current picture – expansion
Russia, the United States and Libya, which have all ratified the Chemical Weapons Convention, are among

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FFI – national centre of excellence

FFI is the only research institute in Norway, with an overall competence in all research and development areas for effective national overall protection against the effect of chemical warfare agents.

Through its long-standing efforts to develop physical countermeasures and medical antidotes against chemical weapons, FFI has developed an overall competence in a wide range of important areas: protective suits, respirators, personal and collective detectors, identification and analysis methods for the detection of chemical warfare agents, threat awareness, knowledge of toxicity, the effect on humans and medical countermeasures, and effective decontamination of contaminated equipment, contaminated areas and persons, etc. FFI is the national laboratory for the analysis of chemical warfare agents and assists in the analysis of toxic industrial chemicals.

This competency has put FFI in a position to strengthen the capability of the Armed Forces to prevent the deployment and consequences of such weapons by ensuring that Norway always has access to effective countermeasures and the institute has helped to strengthen education in this field in Norway – both for military personnel and within the civil sector, including the health authorities.

Cooperation agreements

FFI has entered into a cooperation agreement with the NBC centre at Oslo University Hospital, Ullevål, to promote research and make FFIs knowledge available faster to the wider clinical community in Norway. The NBC Centre was established in 2006 as the national centre of excellence for the medical treatment of persons with injuries after exposure to chemical, biological, and radiological threat agents.

Accordingly, in autumn 2013, FFI entered into a cooperation agreement with the Oslo Agency for Fire and Rescue Services *[Oslo Brann- og Redningsetat]* (OBRE), which amongst other things involves FFI providing technical assistance to OBRE at incidents involving chemical, biological or radiological threat agents and assistance during exercises. The background for the cooperation is the gas spill at Mathallen in Oslo in April 2013 in which FFI provided assistance to identify the cause of the contamination.

STANDARD C-WARFARE AGENTS	POTENTIAL NEW THREATS	BIOREGULATORS	TOXINS	GENETICALLY MODIFIED B-WARFARE AGENTS	STANDARD B-WARFARE AGENTS
Nerve agents Mustard agents Cyanide	Industrial chemicals - Pharmaceuticals - Insecticides	Peptides and proteins	Saxitoxin Botulinum toxin Ricin	Modified bacteria and viruses	Bacteria Viruses Rickettsias

▲ **Figure 1.** Spectrum of the different types of threat agents from chemical to biological warfare agents.

CHEMICAL COMPOUND	LETHAL DOSE ON SKIN	LETHAL DOSE BY INHALATION
Nerve gases		
- *Sarin*	100 - 500 mg	50 - 100 mg min/m^3
- *Soman*	50 - 300 mg	25 - 50 mg min/m^3
- *Tabun*	200 - 1000 mg	100 - 200 mg min/m^3
Mustard gas	7,000 mg	1,500 mg min/m^3
Cyanide	7,000 mg	2,500 mg min/m^3
Chlorine gas	-	60,000 mg min/m^3
Ammonia gas	-	60,000 mg min/m^3

▲ **Table 1.** Overview of the toxicity of some chemical warfare agents and industrial gases.

◂ FFI researcher Bjørn Pedersen pretends he has been exposed to nerve gas during an exercise in 2012. Here he is assisted by FFI researcher and physician Reidar Yngvar Gundersen. *Photo: FFI*

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1. CBRN = *Chemical, Biological, Radiological, Nuclear*. This term is now also used in Norwegian, and has replaced the former Norwegian designation "ABC".

2. Chemical warfare agents include, amongst other things, nerve gases, blister agents, such as mustard gas, blood gases, such as cyanide, lung gases, such as phosgene and chlorine, and a number of naturally occurring poisons (toxins).

3. The nerve gases are amongst the most toxic chemical warfare agents.

4. The standard nerve gases are tabun, sarin, soman, cyclosarin and VX.

5. The nerve gases are liquid but evaporate to form a gas at room temperature.

6. The effect of nerve gases is life-threatening as they inhibit enzymes in the nervous system.

7. Exposure to nerve gas in evaporated form (gas) is the most likely exposure scenario if used against military or civilian targets.

8. Death after nerve-gas exposure is caused by suffocation due to contraction of the airways, the production of mucus that block the airways, fluid in the lungs, inhibition of the respiration centre of the brain and muscle impairment.

9. Development of symptoms after exposure of skin to nerve gas in liquid form takes longer than by inhalation.

10. There are three principles for medical treatment in the event of nerve gas poisoning: Decontamination of the victim, supportive therapy, especially respiration, and injection of several medical antidotes.

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Diagnosis
of nerve gas poisoning

Diagnosis of nerve gas exposure can be performed by clinical examination, laboratory analyses or by trying different drugs. The most obvious symptom of severe poisoning is excessive excretion of mucus in the airways leading to pulmonary oedema. Analysis of various enzymes which are inhibited by nerve gases is possible with the aid of laboratory analyses at FFI or by using automated analyses at the site of the emergency or in hospitals. In 2011, a portable cholinesterase testing system was developed (Figure 3) that allows one to quickly and easily determine AChE and BChE values using only one drop of blood (Securetec Detektions-Systeme AG, Germany). An analysis device of this kind enables rapid and targeted therapy and should be considered for procurement by emergency medical services and the Armed Forces.

▼ **Figure 2.** Auto-injectors used by the Armed Forces and at OUS, Ullevål Hospital. *Photo: FFI*

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Medical treatment
in the event of nerve gas poisoning

Nerve gas is disseminated as a gas or liquid in more or less pure form. Intake into the body occurs via inhalation, skin absorption or via food and drink. Nerve gases are amongst the most poisonous substances we know of and work by inhibiting the enzyme acetylcholinesterase, which breaks down acetylcholine in specific neural connections.

Symptoms and signs of poisoning develop within seconds to minutes and death can occur in a matter of minutes without medical treatment. Small pupils, breathing problems and increased salivation are early signs of nerve gas poisoning.

It is possible that symptoms and the development of muscular convulsions will last for an extended period in the event of exposure to pesticides that are similar to nerve gases. Amongst other things, this is caused by the intake of large doses, for example, in the event of suicide. *For a full description of medical symptoms and treatment in the event of nerve gas poisoning, reference is made to Aas and Jacobsen (2005) and the Handbook of NBC medicine (2008).*

▼ **Figure 3.** Analysis devices for measuring activity of the enzymes acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) from Securetec Detektions-Systeme AG, Germany. This field device can quickly determine whether a person has nerve gas poisoning by a simple and easy blood analysis. *Photo: Securetec AG*

those countries that have declared old stockpiles of chemical weapons. These countries are working to destroy their remaining stockpiles and production facilities. The technology required to develop and produce chemical substances that can be used as effective weapons is relatively simple. However, it is more difficult to develop and produce chemicals with high levels of purity and toxicity.

Furthermore, developing the required efficient delivery mechanisms to disseminate such weapons of mass destruction is resource-intensive. Since many of the relevant technologies are commercially available internationally, it is important that such technology is subject to strict international control. One example of monitoring programmes for chemicals and delivery mechanisms is that established by the Australia Group, which is a group of countries, established in 1985, working to prevent the spread of chemical and biological weapons through monitoring and control of the technologies required for production.

Medical protection

The effect of chemical warfare agents on humans and the medical treatment of injuries after exposure to these substances depend on the type of warfare agent, the toxicity, the concentration/quantity, the duration of exposure, whether the substance is a gas or a liquid, how the substance is absorbed by the body and the health and age of the persons exposed.

For a number of the chemical warfare agents, such as mustard gas, no specific medical antidotes are available, only general therapies prescribed for poisoning with other chemical substances – fresh air, clean water and symptomatic treatment. Even after nearly 100 years of medical research, we have no antidote to mustard gas.

In the case of cyanide poisoning, drugs are available that must be administered quickly after a poisoning event. Similarly, drugs are available that can be used for the emergency medical treatment of nerve gas poisoning, although these are not sufficiently effective to prevent all deaths and injuries.

It is, however, important to determine whether a person is contaminated as quickly as possible. This can be carried out using the electronic instruments available to the Armed Forces today, for example, the Lightweight Chemical Detector (LCD), which detects several of the most common warfare agents, or using simple manual methods developed to detect mustard gas which give a response within a few minutes (Figure 4 next page).

Protection against nerve gas poisoning

Persons with severe injuries after exposure to nerve gas must access medical treatment as quickly as possible. Drugs have been developed for medical protection and treatment, which are reasonably effective against individual nerve gases when administered quickly (Figure 2). The drugs must therefore always be available for use at the site of an emergency and military teams are therefore equipped with auto-injectors for rapid intramuscular administration. In the case of civilian events, these drugs must be made available as part of emergency preparedness, both for use by emergency response personnel at the site of the emergency and in hospital emergency departments. The drugs will increase the chance of survival and reduce the damage to the nerve system after exposure.

Vulnerabilities in current medical protection/preparedness

Existing emergency medical protection against chemical warfare agents is not sufficiently effective to reduce injuries and increase survival rates after an exposure. Today's antidotes are only effective against certain nerve gases and only to a limited extent. International research in this field should concentrate on developing existing treatment protocols against those groups of warfare agents that pose the greatest challenge (Figure 1), in particular the nerve gases. This means developing both more effective prophylaxis for use before exposure and more effective drugs for use in the medical treatment after exposure to nerve gases.

FFI is conducting experimental research in cooperation and dialogue with its NATO partners. We are evaluating international research in this field to develop more effective antidotes to replace those currently available.

This joint initiative in NATO is very significant because one country can't do this work on its own. A recent study by FFI showed that today's antidotes are not sufficiently effective against nerve gases.

Tunnel fires

Experiences from major fires in Norwegian road tunnels, amongst others, has highlighted several deficiencies in Norwegian civil protection emergency preparedness. In the fire in the Gudvanga tunnel (more than 11 km long) in Sogn and Fjordane in August 2013, several patients were treated for cyanide poisoning at Haukeland University Hospital in Bergen. Cyanide or hydrocyanic acid gas is a well-known chemical warfare agent that was used in the concentration camps in Germany during the Second World War. In an incident where such toxic gases are used in terrorist attacks or released as a consequence of major fires, it is imperative that the necessary antidotes are stockpiled in such a way that they can quickly be accessed by healthcare professionals. It is therefore right for the management of the Bergen Hospital Trust *[Helse Bergen]* to point out, in the aftermath of the accident, that stockpiles of antidotes to hydrocyanic gas poisoning must be increased.

Preparedness analysis necessary

On the basis of the uncertainty surrounding Norwegian emergency stockpiles, it is therefore necessary to analyse and investigate whether the size of Norway's stockpiles of antidotes and other necessary emergency preparedness equipment are sufficient and adequate for use in the event of serious incidents at the site of an emergency by Norwegian health authorities. Such an analysis is central to the work to identify vulnerabilities in current civil emergency preparedness and find solutions to enable Norwegian hospitals and emergency response agencies to meet the emerging challenges in the event of an accident in which humans are exposed to different types of chemicals. This will form a basis for establishing, amongst other things, more effective and dynamic medical emergency stockpiles which are also important in the event of terrorist attack.

COUNTRY	PROTECTION TABLETS (PYRIDOSTIGMINE)	AUTO-INJECTOR I		AUTO-INJECTOR II
Norway	x	Atropine	Obidoxime	Diazepam
Sweden	x	Atropine	Obidoxime	Diazepam
Denmark	-	Atropine	Obidoxime	-
USA	x	Atropine	2-PAM	Diazepam
United Kingdom	x	Atropine	P2S	Avizafone
Netherlands	x	Atropine	Obidoxime	Avizafone
Canada	x	Atropine	HI-6	Diazepam
France	x	Atropine	P2S	Avizafone
Germany	x	Atropine	Obidoxime	-

▲ **Table 2.** Overview of medical countermeasures used against nerve gas in some countries. The number of injectors, dosages, types of antidote and combinations of medications in auto-injectors varies

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- The health authorities must evaluate the measures they have implemented and assess whether the emergency stockpiles are adequate at Norwegian hospitals

- Appropriate consideration must be given to prioritising overall national research efforts in the field of biomedical and technological research into improving civil protection

▲ **Figure 4.** Quick test for detecting mustard gas on the skin over 3-10 min. The device is manufactured by Securetec Detektions-Systeme AG, Germany. *Photo: FFI*

▸ The "injured" people are taken to hospital during the 2012 exercise. *Photo: FFI*

Knowledge is important

The authorities at the Ministry of Education and Research should also review the curricula for healthcare professionals and other employees in front-line services to ensure that education and training also include a review of all the challenges and necessary countermeasures in the event of the use of CBRN warfare agents against civilians. Healthcare professionals currently only receive very limited training in this field. This must also be followed up with regular training and emergency response exercises.

National challenges

The latest articles in the news media in August and September 2013 from the Middle East on the use of the nerve gas sarin against civilians in Syria are very serious. The perspectives on the use of weapons such as nerve gases and other hazardous chemicals can seem daunting and can paint a gloomy picture of the future, but the question we must ask ourselves is whether we can or must live with such a threat. By conducting adequate national emergency preparedness measures, including improved collaboration between the Armed Forces and civilian agencies, the consequences of deployment can be managed.

The likelihood of such weapons and warfare agents being deployed in Norway is thought to be low. The reason for this is due mainly to the fact that the warfare agents are difficult for terrorists or equivalent groupings to get hold of, although several chemicals are relatively easy to produce. Other reasons are that there has been a reluctance to deploy these weapons in such groups and that these groups have not mastered the technology required to disseminate these weapons effectively. This reticence is due in part to the fact that such weapons are not easy to handle as most are highly toxic.

We must live with the threat posed by such weapons. Norway's stronger profile as a political player in the international arena over the last twenty years and Norway's role as an important energy exporter also underlines the threat of the use of such weapons. Such a threat not only encompasses Norwegian personnel operating abroad but also civilians in Norway.

The role of the health authorities

Should such weapons be used in Norway, the consequences could be very serious if the authorities do not improve their emergency preparedness. To improve emergency preparedness against chemical weapons, the health authorities should assess whether the emergency stockpiles and the countermeasures to be taken at Norwegian hospitals are adequate. OUS (Oslo University Hospital), Ullevål has established an emergency preparedness plan for the capital and the hospital believes the emergency preparedness situation in Oslo is adequate.

However, a national emergency preparedness analysis should be carried out to assess whether the emergency preparedness in Oslo is sufficient and whether this level of emergency preparedness should also be established at other hospitals in the country. The emergency preparedness measures must include necessary medical preparedness, including physical protection, such as personal protective equipment, equipment for cleaning contaminated persons and technical equipment, such as detectors for identifying chemical warfare agents, etc. This is vital equipment for rescue teams which will help in the aftermath of any terrorist attack. Just as important and necessary for our emergency preparedness is regular theoretical and practical training for all involved teams.

Cooperation between the military and the police

In Norway, the Armed Forces are responsible for external security and the Police are responsible for internal security. Until the terrorist incidents in 2001 in the United States, this was considered to be a relatively clear and appropriate division of labour, although in its 2000 report, the Government Commission on the Vulnerability of Society (Sårbarhetsutvalget) pointed out the need to take a closer look at division of responsibility and cooperation procedures between the Police and the Armed Forces. The terrorist incidents in Norway in 2011 further highlighted this issue and changes were initiated.

Many elements need to be reconsidered, both with regard to division of responsibility, access to resources, remedies, and not least how this new dimension in the challenge spectrum should be prioritised. Appropriate weight must be given to prioritising efforts in several key areas of improving civil protection, including biomedical and technological research. Strengthening this research initiative can make an important contribution to enhanced civil protection.

That is not to say that terrorism supersedes the more traditional challenges represented by threats to use weapons of mass destruction. It is in addition to these challenges.

Research

National and international research into medical antidotes to chemical warfare agents is carried out at public or publicly supported institutions in NATO. Developing countermeasures against a heterogeneous group of chemical threat agents, such as chemical warfare agents, where the probability of an attack and hence the threat of exposure to such chemicals is low, requires long-term public funding. In addition, the market for the sale of such products is very limited. This financing model was prevalent in Norway up to the end of the 1990s when the various political authorities decided that financing should be provided in cooperation with users. The result of this decision is that it appears that no one takes responsibility for research into developing better medical countermeasures and financing is thus gradually reduced along with research and emergency preparedness.

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