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Working Paper on Medical Protection Against Nerve Gas Poisoning (Present Situation and Future Possibilities)

In July 1976 the Yugoslav delegation submitted the working paper CCD/503 to the CCD which contained a comprehensive review of the relevant data regarding the problem of medical protection against nerve gas poisoning.

This working paper, which bears the same title as the one submitted four years ago, endeavours to present the current situation in this field and some investigations that are in progress. Scientific and professional achievements of those countries that engage in active theoretical and practical research in this plane were considered.

1. MODE OF ACTION

Regarding the mode of action of nerve agents, nothing new or important (spectacular) has happened up to date that could alter the generally accepted knowledge.

2. DECONTAMINATION

Concerning decontamination, both personal and total, some armies have succeeded in finding highly efficient decontamination material. It, therefore, seems that the problem of decontamination does not exist any more in its previous form. However, the ingredients that are necessary for decontamination material are very expensive and, having in mind the required amounts, it would not be realistic to expect that -- with the exception of highly developed countries -- the greater part of the world could possess them in sufficient quantities, especially as part of a first-aid kit.

3. ANTIDOTAL THERAPY

Gas masks (or protective masks) and protective clothing can provide effective protection against nerve gas attacks. However, in battlefield conditions, antidotes must be used in the following situations:

- when the lapse of time between the attack and the fitting of the gas mask is more than ten seconds (it is sometimes even shorter when the initial concentration of nerve gas is extremely high);
- when protective equipment does not fit properly;
- when it has been damaged; and
- in cases when the sorptive capacity of the respirator filter or protective suit becomes saturated under conditions which do not permit immediate replacement.

3.1 Atropine still remains the drug of choice. Although some attempts have been made to utilize other compounds instead of atropine (dexetimide and others), none of them were proven to give better protection.

3.2 Oximes. Of the hundreds of oximes that have been synthesized and tested on experimental animals poisoned by nerve gas, only three have found a place in medical practice: pralidoxime (also known as variation P_2S), trimedoxime (known as dipiroxime) and obidoxime (known as toxogenine).

It seems that pralidoxime is losing its priority to obidoxime and trimedoxime because, for some armies, the combination of trimedoxime with atropine and benactyzine is at present the most attractive one. Nevertheless, even this combination does not offer satisfactory protection against one of the nerve agents, i.e. soman.

An important achievement in protection has been made by combining the different routes of oxime application (peroral and intramuscular) in order to maintain an effective concentration of antidotes in the blood for some hours.

3.3 In symptomatic therapy, it seems that diazepam is not in the experimental stage anymore but has become a standard supportive drug in the treatment of convulsions induced by nerve gas poisoning.

It has been calculated that in battlefield conditions an efficient protection against up to 5 LD_{50} of nerve gas poisoning could be offered by using antidotal mixtures that counteract upon the agent which has been used. In view of this, the best protection could be obtained in the case of VX poisoning while it is less effective in case of poisoning by sarin, and less still in case of poisoning by tabun and soman.

4. FURTHER INVESTIGATION

In recent years great efforts have been made in seeking compounds which would provide effective treatment against soman poisoning. Among a number of such compounds, the one coded HI-6 has proven very effective on experimental animals poisoned by soman. However, the HI-6 compound is totally ineffective in case of tabun poisoning.

During the course of the past two years another group of antidotes coded as HGG compounds appears to be the first "universal" oximes, as their application in combination with atropine offers protection against all four standard nerve agents, i.e. sarin, soman, tabun and VX. It should be underlined that HGG compounds are still in the initial experimental stage, while HI-6 is in a more advanced one. It should also be pointed out that a serious setback of the HI-6 compounds is their low stability in water and buffered solutions. Until the stability problem is solved, they cannot replace pralidoxime, obidoxime and trimedoxime in autoinjectors intended for first aid and treatment. It looked as if the problem of oximes of low toxicity which could penetrate the blood brain barrier had a good chance to be solved in 1976. However, this opinion was proven excessively optimistic. The oxime propam was unstable and, what is perhaps even more important, reactivated brain acetylcholinesterase it did not have any remarkable protective advantage over standard oximes in experimental animals poisoned by nerve agents.

The attempt to increase the efficiency of therapy by adding other drugs to atropine - oxime mixture, with the exception of the aforementioned benactyzine, and the separate addition of diazepam, has failed so far. The veratrine-like compounds which seemed so promising in 1976, seem to have also been abandoned.

The United Kingdom delegation presented a paper in 1977 (CCD-541) about the possibility of using carbamates as prophylactic agents against nerve gas poisoning. As far as is known, this work is still in progress.

Another possibility was mentioned in 1976 regarding protection by "shielding" acetylicholinesterase in order to protect critical sites affected by nerve agents. However, no promising results have been obtained until the present.

The previously mentioned activities concerning active and passive immunization seem to be ineffective from the practical point of view.

It was stated in 1976 and should be repeated now, that the continued research in the field of medical protection against nerve gas poisoning is in steady progress, particularly during the last four years when it has made a remarkable step towards its goals.

It is with the greatest satisfaction that it can be said that the first steps in international co-operation of scientific research on prophylaxis and therapy for nerve gas poisoning have taken place. Numerous scientists from various countries met at the Pugwash meetings on Medical Protection against Organophosphorus Poisons Workshops, twice in Yugoslavia and once in Finland. They also met in the German Democratic Republic. On these occasions, they exchanged views, ideas, experiences and results achieved in this field.

As a direct result of the meeting held in 1978 in Yugoslavia (Dubrovnik) the Institut fur Aerobiologie, Grafschaft, Federal Republic of Germany, the Prins Mauritz Lab. TNO Rijswijk, Holland and the Institute for Organic Chemistry and Biochemistry from Zagreb, Yugoslavia organized a control experiment. The aforementioned substance HI-6 was synthetized in each of the three institutes and specimens of it exchanged. The comparing of results obtained in all three institutes including all three specimens showed that there was neither physico-chemical nor biological difference between them in vitro and in vivo experiments.

An increasing number of papers that deal with the protection of experimental animals against nerve agents, especially soman, appear in scientific literature. The most interesting information comes from the Federal Republic of Germany, the Netherlands, Canada, the United Kingdom, Poland and Yugoslavia. However, nothing new or interesting comes from some other countries which are known to have much experience in this field. Some promising publications of this kind are also coming from India, China and some other countries as well.

This brief review is an account of the efforts made by scientists in various countries in seeking the solution for protection against poisoning by nerve agents. Unfortunately, the results show that an efficient antidotal therapy against all four chemical agents mentioned here does not exist for humans.

These facts on how dangerous the use of nerve agents as chemical weapons could be for mass destruction speak for themselves. It is, therefore, the responsibility of all concerned to find the quickest and most effective way to ban chemical weapons.