

Part VI. Other human studies with chemical warfare agents

Overview

Previous parts of the survey describe the main programmes of work involving chemical warfare agents carried out after World War II. To conclude the description of human studies with chemical warfare agents, this part covers the work during World War II (Chapter 17) and miscellaneous work after World War II (Chapter 18). Human studies to develop treatments, often not involving exposures to agents, are covered in Part VII.

The main thrust of physiological research at the start, and in the early years, of the Second World War was offensive. During this period, work was undertaken to improve treatments (Chapter 20) although most effort was aimed at developing new chemical warfare agents, to complement the established ones, and new weapons in which agents could be delivered. Human studies were conducted predominantly with two types of chemical warfare agent: vesicants and harassing agents.

During the early years of the war, many chemical weapons were tested at Porton in field trials. Some trials involved completely new weapon designs, such as aircraft bombs, sprays or glass grenades. Others used traditional weapons (mortar bombs and artillery shells) loaded with new forms of chemical agents, for example, thickened mustard gas. Many of these trials did not involve volunteers; animals or sampling techniques were used to find out the degree of contamination which resulted after the weapon was fired. Other trials did require humans.

Around the end of 1943 and the beginning of 1944, the priorities for research changed. It was recognised that new agents (or variants of established ones) and new weapons could not be produced in time to affect the war in Europe. Instead, the main concern was to ensure treatments were at hand for gases which Germany may use against the Allied invasion. Greater attention was paid to the Far Eastern theatre. It was known that H (mustard gas) was much more effective in tropical climates than temperate (European) ones. Further, treatments for H burns had been found to be less effective on hot and sweaty skin, and impregnated clothing which could protect against H vapour appeared to induce toxic effects if worn for long periods in hot weather.

Thus, from early 1944, research shifted to being wholly defensive. Descriptions of the work carried out to develop treatments and protection for tropical conditions are given in Chapter 20. Chapter 17, therefore, covers predominantly the years 1939 to 1943 and the human studies which were conducted as part of the offensive thrust of research. Two general points might be made.

- There were many hundreds of human studies of the same type carried out during the war. The survey does not describe them all in detail but gives examples.
- The experimental records refer to chemical warfare agents in a variety of ways: chemical name, internal T number or code name. Sometimes the same agent is referred to by different chemical names. To minimise confusion, the code name is used here.

Chapter 18 covers the human studies conducted after 1945 with chemical warfare agents not covered by the previous parts of the survey. There are two parts to this chapter: a description of the work with H, and studies with dye-markers. Work with H after 1945 was predominantly concerned with the further development of treatments and protection (Chapter 20) but some work was conducted which was not. The cessation of the H programme in the late 1970s is covered. Dye-markers had an obvious application for riot control devices but are covered here because they were also developed for training purposes and for use in field trials with simulants.

Chapter 17. World War II

17.1. Introduction

17.1.1. Vesicants

In 1939 the established vesicants were mustard gas (H) and Lewisite (L). Some human studies with vesicants explored the effect on skin [1], a test which involved a small drop, typically of a diameter of 2 mm, of the given liquid being placed on the bare skin of a volunteer's arm. The drop was left in place, the reaction of the skin monitored, and the degree of vesication induced recorded. Vesicant power tests can be split into the following categories.

- Sensitivity studies with H and L The H sensitivity test was used from (at the latest) 1931 as a safety precaution [2]. A small drop of H in a concentration of 1 in 10,000 was applied to the upper arm and the skin reaction noted. Those volunteers whose skin showed a reaction (i.e. were hypersensitive to H) were excluded from participating in any study with vesicants. The H sensitivity test was used in this manner throughout World War II [3] and afterwards but other studies sought to determine the normal reaction to H and L, and to compare the sensitivity of different sites of the body.
- H and L variants Vesicant power tests were conducted with variants of H and L. Different diluents for H and L were considered, as were mixtures of the two and chemical analogues of both. Comparisons were made between the pure agent and the production samples, and between fresh and stored agent.
- Alternatives to H and L Miscellaneous substances were used in vesicant power tests in attempts to find new agents. Typically, a volunteer would have a drop of the new substance placed on his arm, together with a drop of either H or L to allow a direct comparison of the effects. Hundreds of these tests were conducted. The names of the miscellaneous substances used in these tests which induced some reaction are listed in Annex F.

The nitrogen mustards (HN-1, HN-2 and HN-3) emerged during the war. They were not really new vesicants, as they had been investigated before, but interest in them was re-awakened during the war. The nitrogen mustards were considered in vesicant power tests and one study explored human sensitivity to them. Studies in which volunteers were exposed to vapour of H, L or one of the nitrogen mustards were conducted. A few vesicant power tests were undertaken with the "Dick" series of agents.

Table 17.1 shows the various names by which the main vesicants used in human studies were known. It is drawn from a report produced in 1945 [4].

Code Name	Chemical Name	Other names used during the war
H	dichlorodiethyl sulphide	HS
L	chlorovinyl dichloroarsine	
HT (60% H and 40% T)	(T) Di-(β -chloroethylthio)-diethyl ether	T724
HQ (80% H and 20% Q)	(Q) N-carbomethoxy N- β -chloroethyl nitrosamine <i>also</i> N-(β -chloroethyl)-N-nitroso-methyl carbamate	T1792
HN-1	ethyl di-(chloroethyl)-amine	
HN-2	methyl di-(chloroethyl)-amine	S, T1024
HN-3	trichloro triethylamine	T773
ED	ethyl dichloroarsine	Ethyl Dick
MD	methyl dichloroarsine	Methyl Dick
PD	phenyl dischloroarsine	MA

Table 17.1. Main vesicants used in human studies

17.1.2. Harassing Agents

Harassing agents was a term used to cover tear gases and irritant smokes (which were often referred to as nose gases [5]). The main harassing agents [4] used in human studies are given in Table 17.2, which also gives a summary of their effects [5].

Type	Code name	Chemical name	Nature and effects
Tear gas	CN (or CAP)	chloroacetophenone	Non-persistent in vapour form, but persistent in solid form. Induces a stinging pain in the eyes followed by lachrymation.
	BBC	bromo benzyl cyanide also phenyl bromoacetonitrile	Persistent tear gas. Has the same effects as CN, but induces them more quickly.
	KSK	ethyl iodo acetate in alcohol	"Semi-persistent" [5]. Has the same effects as CN but induces them more slowly.
Nose gases	DM (Adamsite)	diphenylamine chlorarsine	Non-persistent. Induces pain in the chest and throat, gums, teeth, forehead and nose in 2 to 4 minutes [5]. Salivation is marked. Induces coughing and possibly vomiting
	DA	diphenyl chlorarsine	As for DM, but the effects are less severe
	DC	diphenyl cyano arsine	As for DM, but the effects are more severe and induced more quickly.

Table 17.2. Harassing agents.

Various miscellaneous compounds were tested in attempts to find alternatives to these harassing agents. The nature of these tests was similar to the method used to find an alternative riot control agent to CN in the 1950s: volunteers were exposed to low concentrations of the compounds in the chamber with any effects noted and compared to known effects of established harassing agents [6]. Often the effect of a compound was compared to BBC. Hundreds of these types of tests were conducted. The compounds used are listed at Annex F. Chamber tests with volunteers also sought to assess mixtures of the harassing agents shown in Table 17.2 and variants of them. Here various concentrations were used.

Using agents to harass enemy forces was a relatively new idea and a range of human studies sought to understand the impact of harassing agents. These studies can be split into investigations of the effects of drops of liquid falling on the skin, and those which explored the effect on performance. The latter studies involved the development of techniques to measure the degradation in performance induced by harassing agents, and to relate that degradation to dosage. A long investigation was conducted into how man might become tolerant to the effects of harassing agents, and the nature of that tolerance.

17.1.3. Other war gases and studies

The established war gases of phosgene, diphosgene and hydrogen cyanide were regarded by Porton as too dangerous to be used in human studies [7] although harmful doses induced only minor symptoms initially. Occasional weapon tests were conducted with these agents in field trials, but these involved either animals or sampling equipment, and even these involved stringent safety precautions for Porton staff [8].

Some human studies were conducted with fluorophosphates and other substances which were known to stimulate the nervous system. While these compounds may not be unrelated to nerve agents, they were tested in the war as harassing agents. None were found to be particularly valuable and, furthermore, some fluorophosphates were known to be difficult to make [8].

17.1.4. Volunteers

A striking feature of human studies during World War II is the regular involvement of volunteers drawn from Porton staff. From 1939 to 1941 all miscellaneous substances tested in the chamber as alternatives to traditional harassing agents involved only Porton staff [8, 9, 10]. Moreover, unlike later years, volunteers were drawn not only from the medical and laboratory staff but most sections of Porton (for example, staff in the photography and administrative sections took part in these chamber trials [9]). Service volunteers began to be employed in testing miscellaneous compounds in 1942 [11].

Porton staff also took part in field trials with harassing agents from February 1941 [12]. Before then, in 1940 and January 1941, volunteers from chemical companies at Winterbourne Gunner participated in these field trials [12]. Volunteers from Porton staff were involved in testing respirators and the physiological load of wearing protective clothing [12].

Porton staff do not seem to have provided volunteers for vesicant power tests or for field trials with vesicants, although it appears common for new members of staff (including women) to have undergone an H sensitivity test [3]. There may be two exceptions to this.

- In 1942 a study assessed the relative sensitivity of skin at different sites of the body to H liquid. The report of the work [13] notes that manual workers and clerks participated but does not say from where they were recruited: they may have been Service volunteers.
- In 1940 a short study was conducted to assess if a low concentration of L could be detected by smell. Although strictly neither a vesicant power test nor a field trial (the study was carried out in the chamber), it did involve a vesicant. The experimental records indicate that Porton staff took part in this study [6].

It would appear that, apart from these instances (and the first is merely a possibility), only Service volunteers recruited under the observer scheme were employed in vesicant studies and field trials [12].

17.2. Human studies with vesicants

17.2.1. H and L sensitivity

Apart from the usual H sensitivity test, which every Service volunteer underwent, a few studies explored the sensitivity of skin to H and L. Since World War I it was "known vaguely that, compared with the skin of the rest of the body, the skin of the hand is relatively insensitive to mustard gas... but no definite attempt to prove ... this impression has been made" [13]. Accordingly, in July and August 1942, [14] volunteers participated in a three-part study.

- Eleven volunteers had a 2 mm diameter drop of H (of a concentration of 1 in 40 in dry benzene) applied to each of 15 sites of the body: forehead, neck, thigh, calf, shin, buttock, chest, back, upper arm, forearm (inner and outer aspect), palm, back of the hand, thumb and ring finger. Each drop was spread over an area of 1.5 cm diameter and allowed to dry. The results showed that the hand and the fingers were "remarkably resistant" and that the inner aspect of the forearm could be considered as representative of the sensitivity of the skin of the body generally.
- Nine volunteers had a single 0.75 mm diameter drop of H applied to the forearm and one drop to the ring finger. The drop was allowed to dry. In all cases there was no skin reaction at the finger, but vesication at the forearm site.
- Tests were conducted with larger drops on the finger only. Fourteen volunteers had a 1.1 mm diameter drop of H placed on the finger, while six others had a 1.1

mm diameter drop of L placed on the finger. No skin reaction was observed in any man.

The report concluded that the hazards arising from handling H were minor, given the insensitivity of the hand and the fingers [13]. An apparent sequel to this work appears in the experimental records but is not covered by the report. In December 1942 six volunteers had a 0.75 mm diameter drop of H applied to each of four sites (upper arm, forearm, back and leg) which were then allowed to dry. Each of the six men developed blisters at these sites.

During the early years of the war, an exploration of the normal reaction of skin to L was conducted, involving 250 volunteers [15]. A 2 mm diameter drop of L was applied to an arm of a volunteer. Before application the arm was dehydrated with alcohol and the surface fat removed with benzene, as the moistness and fattiness of the skin were known to affect the reaction to L [15]. The report of the work [15] notes that concentrations of L used was 1 in 500. Experimental records also include L being applied in concentrations of 1 in 300 [1, 16], 1 in 50 and 1 in 100 [17], as part of the sensitivity work. In all cases, the drop of L was left on the skin for 15 minutes and then the excess blotted off with filter paper [17].

Skin reaction was found to vary greatly [15] and so the tests were repeated with the same subjects. However, this further confused the picture: subjects who showed no reaction in the first test developed erythema in the second, and those whose skin reacted in the first test experienced no reaction in the second. The final phase of the work saw volunteers known to be hypersensitive to H having a drop of L placed on their arm. The results of this work gave no clue as to whether an H hypersensitivity increased or decreased the reaction to L, concluding that skin reaction to L was more varied than the relatively well-ordered reaction to H [15].

17.2.2. Vesicant power tests with variants of H and L

The power tests conducted with variants of H and L are summarised in Table 17.3 which shows the number of volunteers who took part in each test and the number of drops of L (or H) that were applied to their arm.

Agent	Date	Nature of test	Drops	Volunteers
H	Sep 39	Effect of H after storage in bombs and shells [16]	2	4
	Oct 39	Comparison of H and L with a 50/50 mixture of H and L [16]	3	9
	Jan-Apr 40, Jan-Oct 41, Jan-May 42	Chemical variants of H [14, 18, 19, 20, 21, 22]	2-4	178
	Aug 42, Mar 43	Sticky H gel and HT mixture [14, 23]	2	54
	Aug 42	Comparison of undiluted HT and 10% HT in dry benzene or a chloride diluent [14]	4	10
	Aug 42	Comparison of undiluted H and 10% H in dry benzene or a chloride diluent [14]	2 or 3	10
	Dec 42	Comparison of 10% H in petrol and pure H [14]	2	4
	Dec 42	Comparison of H applied as a droplet and as a drop spread over the skin [14]	2	12
	Jul 43	2% H and 5% H mixed with yolk of egg, and 5% H mixed with albumen of egg. Drops applied at various times after mixing [23]	2 or 3	12
L	Jan-Dec 40, Feb-Mar 41 and Nov 41	Comparison of British L with French L, and other chemical variants of L [18, 19, 20, 21].	3	87
	Feb-Mar 41	"Sticky" L (L mixed with pitch and benzene [4])	1 or 2	36

Table 17.3. Summary of vesicant power tests with H and L variants

These vesicant power tests involved only one application of drops to the arms of volunteers. One study was carried out in July 1943 [23] in which drops of H (of concentrations of 1 in 200 and 1 in 20,000) in lubricating oil were applied to the arms, twice daily after washing, for up to 21 days. Twenty volunteers took part in this study. Volunteers were withdrawn from the study before the 21 days were up when their skin had developed severe erythema, and others were withdrawn apparently because their skin showed no reaction to the repeated applications. No report of the study has been found, so its origin and the reasons for withdrawing volunteers are not clear.

17.2.3. Vesicant power tests with Nitrogen mustards

Nitrogen mustards had been considered by Porton before World War II. HN-3 was found to have one tenth of the vesicant power of H and, although the hydrochloride of HN-3 had the useful characteristic of being soluble in water, work had been stopped because the General Staff had no interest [24]. However, interest was re-awakened in HN-3 in 1939 when a French delegation mentioned that HN-3 had some advantages over H, as it was more difficult to detect by smell and had a more powerful effect on the eyes [24].

Similarly, HN-2 had been considered before the war but rejected as the samples of it when evaluated displayed a tendency to decompose [25]. Interest in HN-2 was re-ignited by the suggestion in 1941 that the German "Stickstofflost" agent may have been HN-2, a suggestion given some credence by a patent specification which demonstrated that IG Farben were using HN-2 [25].

These re-awakened interests prompted a range of vesicant power tests with HN-2 and HN-3 in the first half of the war, summarised in Table 17.4.

Agent	Date	Nature of test	Drops	Volunteers
HN-2	May 40, Nov 40	Comparison of HN-2 with HN-3 [18, 19]	3	30
	Feb-Mar 42	Comparison of HN-2 with H [22]	2	32
	May-Jun 42, Sep 42	Comparison of HN-2 and HN-2 hydrochloride [14, 22]	1 or 4	20
	Jul 42	Comparison of H, HN-2 and HN-3 [14]	3	6
	Sep 42	Pure HN-2 compared to production HN-2 [14]	1	18
	Dec 42-Feb 43	HN-2 in various solvents and HN-2 chemical analogues [14]	2 or 4	46
HN-3	Jun 39, Oct 39, Dec 39	Comparison of 3% HN-3 or 5% HN-3 with H [1, 16, 17]	2	36
	Jul 39	HN-3 [1]	2	6
	Jul 39, Jan 40, Jan 41, Nov-Dec 41	Comparison of British HN-3 and French HN-3, HN-3 in various solvents and HN-3 hydrochloride [1, 16, 18, 22]	2 or 5	46
	Sep 39	Comparison of fresh HN-3 and stored HN-3 [16]	2	3
	Jan-Feb 40	Chemical analogues of HN-3 [16, 17, 18]	1 or 3	33
	Nov 41	Comparisons of HN-3 concentrations in formic acid [22]	2 or 4	5

Table 17.4. Summary of vesicant power tests with nitrogen mustards

The vesicant power tests with HN-2 were summarised in a 1943 report which noted that HN-2 had been found to have a vesicant power of a quarter of that of H [25]. The old evaluation of the power of HN-3 was confirmed as being about one-tenth of H [17]. Neither of these results suggested much value in HN-2 or HN-3 as vesicants although, as detailed below, their vapour was found to have some advantages over H.

A few studies were conducted to assess the sensitivity of skin to HN-2 and HN-3.

- In January 1942 [22] 24 volunteers each had a drop of HN-3 in concentrations of 1 in 200 and 1 in 500 placed on their arm. The weaker concentration induced an only minor effect; the stronger one produced erythema in most of the volunteers [22].
- In March 1943 [14, 23] 55 volunteers took part in a comparison of the H and HN-2 sensitivity tests on volunteers who were known to be hypersensitive to H. Forty three volunteers who were normally sensitive to H had one drop of H (1 in 10,000) and one drop of HN-2 (1 in 1000) placed on their arms. No skin reaction was observed. Twelve known hypersensitives had weaker drops placed on their arms (H as 1 in 100,000 and HN-2 as 1 in 5000). Four showed a marked erythema on the site of the H application, but only one had slight erythema on the site of the HN-2 application [23]. No report of the work has been found.

17.2.4. Human studies with mustard vapour

The equivalent of the liquid vesicant power test for vapour involved directing a stream of air containing the vapour of a vesicant at a site on the arm of a volunteer. Typically, the vapour was directed down a tube onto a small area of the arm for a few minutes and the reaction of the skin monitored. Three tests of this nature were conducted and are summarised below.

- In August 1939 fourteen volunteers had a stream of L vapour directed against an area of their forearm for up to 30 minutes. The exposure varied from 200-600 mg.min/m³. Some of the men developed mild erythema [1, 16].
- This work was repeated in August 1943 [23] to determine the dose of L which constituted a hazard to the skin [26]. Twenty four volunteers took part. L vapour was directed down a wind tunnel and the men placed a forearm through a cavity in the side of the wind tunnel, thus placing it in the vapour stream. Four exposure levels were used: 250, 500, 750 and 1000 mg.min/m³, with 6 men being exposed to each. The threshold for vesication was assessed to be 1000 mg.min/m³, as 2 of the 6 men exposed to this level experienced vesication. The lower exposure levels induced only mild erythema among the other 18 men [26].
- An HN-3 vapour study was carried out in December 1939. Six men had vapour directed against an area of one of their arms for either 15 minutes or 30 minutes. The concentration used is not recorded but the effects of HN-3 vapour are noted as being inferior to those which would have been expected with H vapour [17].

One of the disadvantages of H was recognised to be the ease with which it could be detected by smell. Indeed, this was one reason the French were considering HN-3. A series of studies, summarised below, was conducted to investigate how easy it was to smell low concentrations of vesicants other than H. Two of the studies took place in the field but are included here as the later section describing field trials concentrates on work with weapons.

- Two studies were conducted with L. In June 1940 six volunteers were exposed to a concentration of 1.16 mg/m³ for 10 minutes. They experienced no effects but could detect L by smell [27]. Entries in the experimental records suggest that the volunteers used in this study were Porton staff members [6].
- The second study with L was carried out in 1943 and involved 35 Service volunteers. Each volunteer was presented in the laboratory with the smells of HN-2, H and L (in that order). They were told they were then going to be taken outside and asked to try to detect a gas which may or may not be one of those they had smelled in the laboratory. Outside on the Porton range, L was poured over an area of 4 square feet and each man walked past the contaminated ground downwind at a distance of 6 feet. The exposure lasted for about 10 seconds. Only 16 of the 35 volunteers correctly diagnosed the smell (which was akin to that of geraniums) as being of L. Porton concluded that untrained soldiers would not reliably be able to detect L by smell [28].

- In November 1941 five volunteers were exposed to a concentration of HN-3 of 8.5 mg/m³ for 1 minute. They experienced only slight irritation of the nose and the eyes but all mentioned detecting a faint smell of geraniums [29].
- The ability to detect HN-2 by smell was investigated in 1942 although the report of the field trials [25] gives few details. Volunteers were presented in random order with an H simulant (which nonetheless produced the characteristic smell of H), HN-2 and water. All the volunteers recognised the smell of H but the majority of them felt they would have been unable to detect HN-2 by smell without foreknowledge [25].

The effects of H vapour against clothed volunteers were examined in a series of tests in 1941. The volunteers involved wore ordinary service dress and face-pieces to protect their eyes [20, 21] and remained in the chamber for long periods with breaks for meals. The tests are summarised in Table 17.5 [20, 21]. In addition to these tests, a study in March 1942 involved a shorter exposure of 1 hour but to a higher concentration of 31.2 mg/m³. Six men took part.

Date	Exposure details	No. of men
June 1941	Men in the chamber for 7 hours with 2 breaks of 30 minutes for lunch. Average concentration 0.27 mg/m ³	4
July 1941	Men in chamber for 6 hours with 90 minute break for lunch. Average concentration 0.6 mg/m ³	4
July 1941	Men in chamber for 4 hours. Average concentration 0.9 mg/m ³	4

Table 17.5. H vapour exposures to clothed men 1941.

The effect of HN-2 vapour against clothed men was investigated in March 1942 [22]. Six men, wearing battle dress and respirators, were exposed to a concentration of 30 mg/m³ for one hour daily on up to 5 consecutive days [22, 25]. The progression of the work is summarised below [25].

- After 2 exposures, erythema had developed in the armpit and on the scrotum of one man. Another man had erythema of the armpit and on the scalp, and a third had slight erythema on the scrotum. These 3 men were withdrawn from the study.
- After 4 exposures, one man remained unaffected but the other two remaining men had erythema on the scalp and scrotum.
- None of the six men were deemed to be casualties after these exposures to HN-2. However, all six were subsequently exposed to H vapour (at the same concentration over the same length of exposure). Following this exposure all 6 men were deemed to be casualties, 3 being severe casualties due to scrotal burns.

The term 'casualty' seemed to have a precise meaning: a man who was unable to take part in military operations for a minimum period of 1 to 2 weeks. As described in Chapter 20, six volunteers who took part in a study of the effect of H vapour on the scrotal region sustained injuries of "casualty severity" [31]. The men were unfit for duty for 7, 10, 10, 28, 28 and 28 days respectively. In the section later in this chapter dealing with field trials, some volunteers participating in trials with vesicant weapons sustained burns considered to be of casualty severity and many were unfit for duty for 32 days [32].

Therefore it might be inferred that the six volunteers who took part in the HN-2 study summarised above, who became casualties after the exposure to H, were unfit for duty for at least 1 to 2 weeks, with the three severe casualties being unable to perform military duties for longer. As mentioned in Chapter 20, some of the studies which considered treatments for

vesicant burns involved 31 casualties [33]: 14 of the cases arising from exposure to vapour and 17 from exposure to liquid.

The effect of L on clothed men was assessed in a field trial in 1943 [26]. Three groups of 6 men were exposed to L at levels of 400, 700 and 1500 mg.min/m³ respectively. The men wore normal battledress and respirators during the exposures, and continued to wear the battle dress for 6 hours afterwards. Only one man, in the group exposed to 1500 mg.min/m³, showed a reaction to the vapour by the development of vesication on his neck [26].

Assessments of eye effects were the final form of vapour study conducted. Tests with H vapour against the eye were conducted in 1941 and are summarised in Table 17.6 [21]. The men wore normal service dress and oro-nasal respirators to protect their respiratory passages [21].

Date	H concentration (mg/m ³)	Length of exposure	No. of men
Jul 41	0.9	30-45 minutes	4
Aug 41	0.102	8.5 hours	4
Aug 41	0.112	2 hours	4
Aug 41	0.102	8 hours daily on 3 successive days	4
Aug-Oct 41	35.5	3 minutes	7
	68.6	60-90 seconds	7
	137.3	60 seconds	6
	343.2	15 seconds	3
	0.23	2.5 hours	8

Table 17.6. H vapour exposures to eyes.

No report has been found of the results of this work. The exposure levels employed range from 3 mg.min/m³ to 106.5 mg.min/m³. A subsequent report, comparing the eye effects of HN-1 and H, notes that 90 mg.min/m³ is about the lower limit of the bracket of exposures which would render a man unfit for his usual duties (shooting a rifle or driving a truck) [34]. A report comparing HN-2 with H, published in 1943 [25], notes that the exposure level of H to induce casualties from eye effects is 100 mg.min/m³. It might be inferred from these figures that the study with H conducted in 1941 involved some exposures at levels below that necessary to induce casualties but within the lower limit.

The effect of HN-2 on the eyes was considered in 1942. Men "were exposed to various nominal concentrations of S [HN-2] vapour for varying times until a conjunctival reaction was observed" [30]. The report does not make clear how many volunteers took part. The initial exposures to HN-2 used were:

- 6.5 mg/m³ for 5 minutes (32.5 mg.min/m³);
- 13 mg/m³ for 5 minutes (65 mg.min/m³);
- 30 mg/m³ for 3 minutes (90 mg.min/m³);
- 4 mg/m³ for 20 minutes (80 mg.min/m³).

Conjunctival reactions were observed after the third exposure and therefore a second series of exposures was designed. However, "considerable technical difficulties about the behaviour of S [HN-2] in the chamber ... made it impossible to forecast the establishment of a given concentration of S ... therefore, it was thought advisable to discontinue the exposures as the variation in concentration was beyond the limits of safety" [30]. As examples, a concentration intended to be 30 mg/m³ was attempted but found to be 14 mg/m³, and an intended concentration of 4 mg/m³ transpired to be 5.5 mg/m³.

The observations made by the study were:

- at exposures of 40-55 mg.min/m³ symptoms (a feeling of grittiness beneath the eyelids and lachrymation) were noted 8-15 minutes after the men left the chamber;

- a second phase of symptoms was experienced 6-10 hours after exposure, consisting of pain sufficiently strong enough to prevent sleep, lachrymation, sensitivity to light and blepharospasm;
- symptoms in this second phase lasted for about 6 hours, with the exception of the pain which was still present (though less severe) 24 hours later.

The study concluded that HN-2 at 40 and 55 mg.min/m³ was the lowest limit of exposure required to induce casualties but that "for offensive purposes a minimum [exposure level] of 70 mg.min/m³ should be aimed at" [30]. A report summarising the effects of HN-2 noted that an exposure level of 100 mg.min/m³ would induce casualties through eye effects alone [25].

The effect on the eyes of HN-1 was explored in 1943 [34]. Checks were made before each exposure so "the danger of an over-exposure and consequent serious damage to the observer's eye was therefore negligible" [34]. Volunteers were given a full ophthalmic examination before the study and "any observer showing acute or sub-acute deviations from normal were rejected as unsuitable for the experiments" [34].

The 21 volunteers who took part wore respirator face-pieces modified so that HN-1 vapour passed over the eyes while the volunteer breathed pure air. The right eye was protected with gauze and a plaster and the volunteer was told to keep his left eye open during the exposure. The exposure levels used in the study varied from 37-90 mg.min/m³ (t varied from 5-60 minutes). The study noted the following [34]:

- it was difficult to find an absolute relationship between exposure level and effects, but no eye lesions or symptoms were observed below an exposure of 41 mg.min/m³;
- exposures exceeding 52 mg.min/m³ produced mild corneal changes in every volunteer, but often the men felt no symptoms;
- at 90 mg.min/m³ one of the three men was considered a casualty, and the other two had symptoms for 4-5 days and one of those had definite corneal damage;
- the average interval between the exposure and the onset of symptoms was about 13 hours and the most common lesions observed were minute greyish-white flecks which disappeared spontaneously in 1-15 days.

The study concluded that an exposure level of 90 mg.min/m³ of HN-1 was about the lower end of the casualty-inducing zone. The work explored the eye effects of HN-2 in rabbits and extrapolated results to suggest that the casualty threshold for HN-2 against the human eye would vary between 21-89 mg.min/m³, depending on the duration of the exposure [34].

17.3. Harassing Agents

17.3.1. Mixtures and variants of harassing agents

Numerous tests in the chamber were conducted with variants and mixtures of established harassing agents (the substances tested are listed at Annex F). Many were carried out with volunteers drawn from the Porton staff; those tests which involved Service volunteers are listed in Table 17.7 [6, 11, 35]. The table lists the substances (as given in the experimental records) and the concentration(s) used.

Unless stated, volunteers who took part were exposed to each combination of substance and concentration. Thus the first test, which lists three substances and 2 concentrations for each, involved a total of 6 exposures for the men who participated. Normally the exposures lasted for less than 5 minutes, if the men could tolerate the substance for that long. Otherwise they were allowed to leave [22].

Date	Substance	Concentration	No. of men
Jul 41	m-acetyl DA and m-acetyl DC	1 in 100 million & 1 in 200 million	6
	m-chloroacetyl DA	1 in 20 million & 1 in 100 million	
Aug 41	pure o-nitro CN, mixed nitro CN, pure CN	1 in 100 million	5
Sep 41	DA variants (methyl diphenyl chloroarsine-3-carboxylate, diphenyl chloroarsine-4-carboxylic acid, methyl diphenyl chloroarsine-4-carboxylate)	1 in 100 million	5
Oct 41	DC variants (methyl diphenyl cyano arsine-3-carboxylate, methyl diphenyl cyano arsine-4-carboxylate)	1 in 10 million	4
Oct 41	4 methyl w-CN	1 in 100 million	4
Oct 41	o-nitro CN	1 in 100 million	6
Oct 41	m-nitro CN	1 in 25 million	5
Nov 41	6-nitro-3-acetamido-w-CN	1 in 10 million	10
Nov 41	w w CN	1 in 100 million, 1 in 10 million, 1 in 1 million	5
Dec 41	crude nitro CN	1 in 5 million, 1 in 100 million	24
Dec 41	pure o-nitro CN	1 in 5 million	40
Jan 42	4 nitro-3-acetamido CN, 4 nitro-3-amino CN, 3-amino-w-CN hydrochloride	1 in 10 million	5
Jan 42	2:4-dimethyl w-CN, 2:w-di-CN	1 in 10 million & 1 in 100 million	10
Jan 42	4:w-di-CN	1 in 10 million & 1 in 100 million	5
Jan 42	2-hydroxy-5:w-di-CN	1 in 10 million & 1 in 100 million	5
Feb 42	o-chloro- α -BBC	1 in 100 million, 1 in 20 million, 1 in 10 million	5
Feb 42	DC mixed with nonoyl vanillylamide	1 in 20 million	5
Mar 42	o-nitro BBC, p-nitro BBC	1 in 100 million & 1 in 10 million	10

Table 17.7. Variants of established harassing agents tested with Service volunteers.

17.3.2. Effects of drops of harassing agents

In a similar way to the skin tests carried out with CS and CR in the 1960s (Part V), some harassing agents were applied to the skin of volunteers to find out if they caused any irritation; these tests are summarised in Table 17.8. The experimental records are unclear on how long the liquid remained on the skin although the DM was left on the skin for up to 15 seconds [20].

Date	Agent	Site used	Drop	No. of men
Jun 40, Nov 40-Feb 41	BBC	arm	One drop of either 1.1 mm or 2 mm diameter	69
Mar 41	DC	arm	One 0.75 mm diameter drop	3
Jun 41	DM	arm	One 0.75 mm diameter drop	3
Jul 41	BBC	shaved cheek	One 0.5 mm diameter drop	3
Jan 42	KSK	arm	One 2 mm diameter drop	24

Table 17.8. Skin reaction tests with harassing agents.

A series of studies was conducted to investigate effects on the eye of drops of harassing agents. Some of the studies sought to replicate the situation where soldiers had been contaminated with liquid harassing agents and had then donned their respirators, thus trapping inside the respirator any drops which may have fallen on their face. Inside the respirator, the vapour from the drops would then induce eye effects [36].

The following technique was used [21, 36]. Drops of the liquid harassing agent under test would be placed on a piece of cellophane. The cellophane (with the drops facing away from the skin) was then fixed to the face of a volunteer with plaster. This procedure prevented the drops coming into contact with the skin of the face. While the cellophane was being applied to his face, the volunteer was instructed to keep his eyes closed. His eyes remained closed

while his respirator was donned and adjusted. The volunteer opened his eyes and over the course of the next few minutes (typically, 3 minutes) [19, 20] the effects induced by the vapour from the drops of liquid were recorded. The time for the following effects to develop (if they did) was recorded: irritancy, tear formation, lachrymation and blepharospasm [20].

This technique was most commonly used when several drops were applied. In some studies only a few small drops were applied and, in these cases, they were applied directly onto the skin of the face. The respirator studies summarised in Table 17.9 [17, 19, 20, 21, 22] show whether the drops were applied to the bare skin or on cellophane.

In 1940 ethyl chloroformate and 1-nitropropene had been tested in the chamber with volunteers from the Porton staff [35] before they were trialled further in the respirator tests listed in Table 17.9. The agents were tested again with Service volunteers in 1945 [35] but no reference to them has been found in reports. It might be assumed that they emerged from chamber tests as promising alternatives to established harassing agents. On the other hand, ethyl chloroformate was used in later respirator tests in a mixture with CN, so it is possible that it was investigated on its own in the respirator test of March 1941 to establish its effect. That might have aided researchers understanding of the contribution made by CN and ethyl chloroformate when applied as a mixture.

Other studies of the effect of vapour from drops of harassing agents were carried out involving large numbers of drops placed on normal Service dress worn by volunteers, who then walked around in the open air. These studies are summarised below.

- In February 1941 [20], three volunteers had 10 or 20 drops (3 mm diameter) of BBC placed on the shoulders of their Service dress and walked around in the open air. Another 17 volunteers had 60 drops (0.75 mm diameter) placed on the shoulders of their Service dress.
- Also in February 1941 [20], four volunteers had 135 drops (0.5 mm diameter) of thickened BBC placed on the collar and back of their Service dress and walked about in the open air. A further 6 volunteers repeated the process, with 140 drops after which they went to a heated chamber.

Date	Agent	Applied on	Drops	No. of men
Jun-Dec 41	BBC	skin	One 0.5 mm drop on the jaw	8
	BBC (with German and Italian facepieces)	skin	Up to six 0.5 mm drops on the cheek, nose, chin and forehead	12
	BBC	skin	Ten 0.5 mm drops on the cheek, nose, chin and forehead	27
Dec 40	1-nitropropene	skin	Three to six 0.5 mm drops	4
Jan-Feb 41	KSK (comparison of British and German respirators)	skin	Up to six 0.5 mm drops on cheek, nose, chin and forehead	12
	BBC (comparison of British and German respirators)	skin	Up to six 0.5 mm drops on cheek, nose, chin and forehead	6
Mar 41	Ethyl chloroformate	cellophane	Thirty 0.5 mm drops over cheeks and nose & ten 0.5 mm drops on the chin	6
July 41	Comparison of BBC and CN/methylene chloride mixture	cellophane	Thirty 0.5 mm drops over cheeks and nose & ten 0.5 mm drops on the chin	12
Jun-Jul 41	Comparison of BBC, BBC and CN mixtures (70/30 and 90/10)	cellophane	Thirty 0.5 mm drops over cheeks and nose & ten 0.5 mm drops on the chin	12
	CN in ethyl chloroformate (10% and 25% CN)	cellophane	Thirty 0.5 mm drops over cheeks and nose & ten 0.5 mm drops on the chin	8
	CN in crotonaldehyde	cellophane	Thirty 0.5 mm drops over cheeks and nose & ten 0.5 mm drops on the chin	3
Jul 41	BBC	skin	One 1.1 mm drop applied on each cheek and then either left or wiped off with the hand or wiped off with a cloth	9
Aug-Sep 41	BBC compared to CN/ethyl chloroformate mixture	cellophane (see Note 1)	Two 1.1 mm drops below each eye	10
		cellophane (see Note 2)	Three 1.1mm drops on nose and cheeks	9

Note 1. Each piece of cellophane was left in place under the respirator for 20 minutes and was then transferred to another volunteer who wore it under his respirator for another 20 minutes.

Note 2. The volunteers in this test either opened their eyes immediately after the respirator had been donned or waited 15 minutes before doing so.

Table 17.9. Eyes effects of drops under respirators.

The final study of the effect of liquid agents was conducted in November 1941 [35] and involved a drop being applied directly to the eye. Each drop was made up of the agent (to a certain concentration) in 85% saline. Eight volunteers had a single 2 mm diameter drop of BBC placed in their eye: 2 volunteers for each concentration of 1 in 10 million, 1 in 2 million, 1 in 1 million and 1 in 100,000. The tests were repeated with another 8 volunteers with the same concentrations of CN.

The effect of flushing the eye immediately after the drop was instilled was investigated for BBC drops of concentrations 1 in 10 million, 1 in 5 million and 1 in 2 million, and for CN at a concentration of 1 in 2 million. Four volunteers had a single drop of one of these concentrations instilled into one eye [35].

17.3.3. Impact on performance

The value of harassing agents was assessed in many field trials in 1940 and 1941. Typically, volunteers would be positioned at some distance from a generator which produced a cloud of the harassing agent. They would remain there for a few minutes and then complete a task which measured the effect the agent had on their performance. The pegboard test was commonly used: wooden pegs with numbers on them had to be pushed into numbered holes in a board.

Work carried out in 1941 to assess the value of DA, DC and DM as offensive agents featured field trials and, uncommonly, a surprise attack on troops participating in an exercise [37]. The work also included chamber tests in which volunteers from Porton staff participated. The main elements of the work are described below [37].

- Field trials Through May and June 1941 a series of field trials was conducted. A group of 6 unprotected men were positioned some distance from a generator, with another 6 further away (to experience a lower concentration). The concentration produced by the generator was controlled and the men stayed in position for up to 3 minutes. They were allowed to don their respirators if they found the effects intolerable. Exposures to DA varied from 10-90 mg.min/m³; to DC from 2.5-22.9 mg.min/m³; and to DM from 14-120 mg.min/m³. In all 198 men took part. At most, half the men were incapacitated for up to 10 minutes after their exposure but many experienced only negligible effects.
- Chamber tests Volunteers in groups of 3 were exposed to a concentration of 1 in 1 million of DA, DC or DM. They entered the chamber wearing respirators and, once the cloud of agent had been mixed properly, removed the respirators for 2 minutes. The volunteers then performed the pegboard test, sometimes inside the chamber and sometimes outside. In all 124 Service volunteers and 48 civilian staff members took part. The report of the work does not cite the results of the pegboard tests.
- Exercise To assess the value of DM against troops, a surprise attack was mounted in the early morning against soldiers on an exercise. The report does not indicate where this was carried out. DM at a concentration of 1 in 100,000 was generated over the soldiers. They recognised the nose symptoms and donned their respirators within 30 seconds. Three men did not (two remained asleep and were not awakened by the initial effects of DM until they had inhaled enough to be sick). The effects of DM in these three men subsided within an hour.
- Unexpected exposures During the exercise civilians were accidentally exposed to DM. About 2400 yards from the DM generator and on the fringe of the DM cloud it produced, a number of civilians including children aged from 6 weeks to 10 years were living in caravans. The concentration of DM at the caravans was estimated as being "considerably less than 1 in 1 million". Interviewed later, one man living in the caravan explained that the children had reacted to the gas first, waking up coughing and crying. He and his wife concluded they were experiencing gas but did not put on their respirators. The effects lasted for 30-45 minutes and all were well enough to eat their breakfasts later. Another group of civilians in buildings near to the caravans detected the gas and put on their respirators. They experienced no ill effects, other than some slight coughing because of the difficulty of persuading their children to do the same.

The report of the work concluded that DM would be unlikely to harass soldiers who were aware of the threat of gas and who reacted, as trained, to put on their respirators. Porton clearly felt the methods used in these types of field trials were too subjective to assess the value of harassing agents properly, for work began in 1942 to develop tasks to objectively measure the decrease in performance the agents induced. Different tasks were developed for tear gases (BBC, CN) and irritant smokes (DA, DC and DM).

For tear gases, which affected vision, the task used to measure performance needed to be sufficiently difficult to be near the limit of a subject's visual capacity [38]. To this end the rangefinder task was devised as detailed below.

- The subject looked down a tube at a photograph of an aircraft. The right half of the photograph was viewed through a thin sheet of glass at the far end of the tube.
- During the task the sheet of glass rotated slowly, refracting the image seen by the subject. The subject had a lever to correct the error in the view of the aircraft.
- The lever and the rotating glass mechanism was a sensitive piece of equipment and it was easy for the subject to over-compensate. Further, the rotation of the glass combined with adjustments of the lever to make the refractions seen in the photograph unpredictable. The task lasted for about 3 minutes.

In the spring of 1942 the rangefinder and pegboard tasks were compared as ways of measuring the impact on performance of BBC [38].

- Volunteers performed the pegboard task before exposure to BBC, during exposure (as the concentration rose to either 1 in 10 million or 1 in 20 million) and after exposure. Some volunteers, who served as controls, were exposed to an innocuous gas (toluene) instead of BBC. In all 47 volunteers took part.
- Ninety two volunteers performed the rangefinder test. They were exposed to BBC under their respirators. Fifteen 1 mm diameter drops of BBC were placed on cellophane and this was attached across the nose and cheeks. The respirator was donned. Some volunteers (who served as controls) had cellophane attached to their face on which water instead of BBC had been placed. All volunteers completed the rangefinder task in advance, with and without respirators, and again two minutes after the BBC had been applied.

The rangefinder task was found to give a more consistent measure of performance than the pegboard test (which was not a difficult task visually) [39]. The rangefinder task was sufficiently accurate for Porton to use to produce "harassment curves" for BBC and CN in 1943. These curves related the percentage of men who could be expected to be incapacitated by the dose to which they were exposed. The curves allowed the critical concentration for a tear gas to be found, defined as "the concentration above which no further increase in concentration will produce any further degree of harassment" [35]. Typically, the critical concentration produced immediate blepharospasm. A summary of the work conducted to find these harassment curves is given below [35].

- BBC vapour Eight concentrations of BBC were used, varying from 1 in 200 million (0.04 mg/m^3) to 1 in 500,000 (17.4 mg/m^3). Thirty six men were exposed to each concentration (giving a total of 288 participants). Each volunteer carried out the rangefinder task five times (a learning run, a measured run, once during the exposure to BBC, and twice afterwards). The critical concentration of BBC was found to be 0.6 mg/m^3 .
- BBC liquid contamination BBC could be delivered in droplet form against enemy troops and previous work had suggested that a ground contamination density of 0.15 g of BBC per square metre was necessary to produce effective harassment. The density of droplets (delivered, for example, by spray from an aircraft) producing this ground contamination would be such that 1.5 mg of BBC liquid could fall on the face of a man [35]. The cellophane and respirator technique was used. Six different formations of drops were considered, varying from a total of 0.8 mg to 8.8 mg. Each drop formation was tried with 36 men (giving a total of 216 participants). Each volunteer carried out the rangefinder

test five times. The harassment curve produced suggested that 50% of men would be harassed by 1.6 mg of BBC falling on their face.

- CN vapour The method used to establish the critical concentration of BBC vapour was repeated for CN. Six concentrations of CN were used, varying from 1 in 100 million (0.6 mg/m^3) to 1 in 1 million (6.9 mg/m^3). The CN critical concentration was found to be 0.7 mg/m^3 .

The rangefinder task was not suitable to measure the degradation in performance of irritating smokes such as DA, DC and DM. These did not affect the eyes in the same way as tear gases but the effects they did induce (see Table 17.2) might be expected to degrade physical performance and have a greater influence on motivation [40]. An investigation was carried out in 1942 into the tasks that might be suitable for irritant smokes.

The first phase consisted of chamber tests in which volunteers were exposed to DC (at a concentration of 1 in 20 million), BBC (1 in 10 million or 1 in 20 million) or an innocuous gas (either toluene or methyl salicylate). The exposures lasted 40 minutes. During that time the men completed five tasks [40]:

- the "triple tester" which tested hand/eye co-ordination through having the subject control a pointer along a zigzag path by means of a wheel;
- the pegboard test;
- stepping on to and off a chair 20 times a minute for 3 minutes;
- a spotter test, in which the subject was shown photographs of aeroplanes and had to say where in the photograph the aeroplane was positioned;
- a picture classification test, in which the subject had to stipulate the nature of the object depicted.

The study featured 72 men: 25 were exposed to DC, 19 to BBC and the remainder served as controls. The tests were found to be unsatisfactory as the men were neither motivated to complete them nor did they tax the strength. An assault course was thought to overcome these disadvantages and two trials were conducted in which men completed the course twice; once before and once after a 2 minute exposure to DA. The first trial employed rested men, the second tired men.

Rested men The 139 volunteers who took part were split into teams of four (with one team of three). To increase the motivation of the men monetary rewards were offered: "The men were told that each of the teams would run separately and a record would be made of the time taken by each man to do the course before and after the gas. These scores would be averaged and in each team the best man would receive 6/-, the second man 3/- and the third 1/-. Everyone should try to finish the course because all those who did it satisfactorily on both occasions would qualify for a draw in which rewards of 5/- each would be allotted" [40]. The trial is summarised below [40].

- Before the second run the men were exposed to DA (average concentration 26.6 mg/m^3), or a non-toxic smoke (hexachlorethane). Each of the two groups was split into two, with one sub-group completing the assault course while wearing their respirators. The other sub-group did not wear respirators.
- Two men refused to take any further part after the first run over the assault course, and before being exposed to gas. The remaining 137 men were exposed to smoke; 67 to DA.

- The respirator was found to aggravate the breathlessness and choking feeling induced by DA. The majority of the men were clear of symptoms about 10 minutes after finishing the assault course, which took 2-5 minutes to complete.

Tired men. The aim of this trial was to investigate the effects of DA on men who were physically tired and dispirited, which might be more realistic battlefield conditions. Fifty two infantry men from the 16th battalion of Royal Fusiliers took part. The development of the trial is summarised below [40].

- For 7 of the 10 nights before the trial the men had no more than a few hours broken sleep. On the day of the trial, they were given an easy morning and afternoon. The volunteers arrived at Porton at 8 o'clock in the evening.
- Soon after they arrived they completed their first run over the assault course. At 10 pm the men began patrols over the neighbouring woods. Their company commanding officer inspected them from time to time to make sure none of them slept. At 4 am the men began a 15 mile march in full equipment, returning about 9 am.
- The men had had no food for 14 hours and were "cold and tired and hungry". They were then exposed for 2 minutes, either to DA (mean concentration 9.8 mg/m³) or to hexachlorethane, and tackled the assault course a second time.

DA was found not to be an effective weapon under these conditions, even against tired men. A third of the men exposed to DA were definitely slower over the assault course than their first run but not seriously harassed. Six of the 95 men exposed to DA in these trials collapsed but quickly recovered [40]. The study concluded that the assault course was a suitable method for testing the performance degradation induced by irritant smokes.

17.3.4. Studies of tolerance

Studies in 1925 had shown that men exposed to CN at a concentration of 1 in 5 million became tolerant of the effects after about 1.5 minutes [41]. A study in 1941 explored this development of tolerance [41]. Volunteers were exposed to various concentrations of BBC and CN, varying from 1 in 1 million to 1 in 200 million. At each concentration different volunteers were used. The study found that "tolerance was readily obtained" by remaining in the tear gas atmosphere and tolerance usually lasted about 45 minutes.

Some volunteers in the study were exposed to CN and then BBC. In the first exposure they remained in the tear gas until they could tolerate its effects. At various intervals after that they were then exposed to the other tear gas. The report concluded that "tolerance once established for one tear gas [CN] holds good for another (BBC)" [41].

Studies of the development of tolerance to irritant smokes were conducted in 1941. In the first set of tests volunteers were exposed to low concentrations of DC (from 1 in 150 million to 1 in 50 million) for 30-45 minutes [42]. The effects of DC were found to wear off. This development of tolerance to DC was investigated with short exposures to high concentrations of DC [42], as outlined below.

- Twelve volunteers entered the chamber, containing a concentration of DC of 1 in 4 million, wearing their respirators. After the DC had been mixed properly, 6 men removed their respirators for 15 seconds, the other 6 taking off their respirators for 30 seconds. The men left the chamber and completed the pegboard test.
- The procedure was repeated 30 minutes later and subsequently at the same intervals, until the men had been exposed five times. On each occasion fresh DC was put up in the chamber.

- Successive exposures to DC were found not to have a cumulative effect. Indeed, the results suggested that even for short exposures some degree of tolerance was acquired.

A longer study into tolerance was conducted in 1942 [43], in a series of chamber tests with BBC and CN. The tests are outlined below [43].

- Twelve men were exposed to a concentration of BBC of 1 in 10 million for 60 minutes. Lachrymation and spasm of the eyelids stopped in all men after 3-10 minutes. Five subjects relapsed later in the exposure but only to the extent that their eyes filled with tears.
- Twelve men were exposed to 1 in 5 million BBC for 75 minutes. All were tolerant by 7 minutes into the exposure (i.e. lachrymation and blepharospasm had ceased). After 25 minutes, the concentration was boosted with another 1 in 5 million BBC. Four of the men were affected with lachrymation and blepharospasm. However, tolerance was reacquired some minutes later. With 10 minutes remaining of the exposure, 1 in 5 million CN was introduced to the atmosphere of the chamber. All the men experienced marked blepharospasm within 2.5 minutes. To test the duration of tolerance the men were exposed to 1 in 50 million BBC 4 hours after the 75 minute exposure. Lachrymation and mild blepharospasm were observed in all.
- Twelve subjects completed a re-run of the previous test but with BBC and CN reversed. The effects observed were similar. The introduction of BBC to the atmosphere after tolerance to CN had been acquired induced harassing effects.
- Six volunteers were exposed for 30 minutes to BBC. Initially the concentration was 1 in 50 million but at 5 minute intervals the concentration was boosted by another 1 in 50 million. Only one subject had a relapse of tolerance.
- Fourteen men were exposed to 1 in 5 million BBC and removed from the chamber once they had become tolerant. They were then returned to the atmosphere at various times later to find out how long their tolerance lasted. They remained in the chamber for 5 minutes for the second exposure.

These tests suggested that tolerance could be broken either by a change in the character of the tear gas atmosphere (such as the introduction of CN into an atmosphere of BBC) or by a sudden increase in the concentration of the tear gas in the atmosphere. Further tests were conducted with CN and BBC to confirm this. The time taken to develop tolerance varied enormously: some men became tolerant after as little as 2 minutes, while others required 40 minutes to get used to the effects.

The final tests of the study saw men repeatedly exposed to BBC or CN to find out if the effects lessened as experience grew [43].

- Eight men were exposed to 1 in 10 million BBC for a few minutes at 30 minute intervals for a total of 9 exposures. The symptoms experienced by the men became progressively less marked from the fourth exposure onwards.
- Six men were exposed to 1 in 5 million CN for a few minutes at 30 minute intervals for 7 exposures. The symptoms lessened from the fifth exposure onwards.
- Finally, 8 men were exposed to 1 in 5 million BBC every 30 minutes for 8 exposures. Symptoms grew milder from the third exposure.

17.4 Field trials of weapons

17.4.1. H weapons

Many weapons were tested at Porton, often without the participation of volunteers. Some of the trials were technical design tests and some tested the concentration and pattern of dispersion of agent from chemical weapons (many using samplers or animals). However, some tests of mustard gas weapons did involve Service volunteers.

In October 1941 [44] a trial was conducted to analyse the "initial cloud" expected from H weapons and the effect it would be expected to have on humans. The conduct of the trial is outlined below [44].

- Eleven chemical mines containing H were spaced across wind at 10 yard intervals. Two sampling lines, 100 yards and 150 yards away, were populated with 10 volunteers spaced at 10 yards intervals. The men hid in a sandbag shelter when the mines were exploded and then ran to their sampling position.
- Each of the men was protected by impregnated trousers, rubber boots, respirator and hood, and gloves. Each wore a regulation shirt, from which a window measuring 3 inches by 4 inches had been cut to expose the skin. Each man had a piece of detector paper attached to his respirator and to his chest.
- After arriving at their position on the sampling lines, the men remained until the cloud of H had passed. They then removed their gloves, respirators and hoods. The men who had stood at the 100 yard sampling line continued to wear the remainder of the clothing for four hours after the trial. Those who had stood on the 150 yard line wore their clothes all night and removed them 16 hours later.
- The average concentration of H at the 100 yard sampling line was found to be 72 mg/m³, and 27 mg/m³ at the 150 yard sampling line.

Only two men "escaped any kind of skin damage". Eight men developed lesions of casualty severity and their treatments were started immediately. Two of these men developed fresh blisters around the site of their previous lesions and were admitted to hospital 8 and 11 days (respectively) after the trial. In these 8 men, vesicles appeared not only on the skin exposed through the window cut in their shirts but also on the skin which was protected by battledress. The delayed effects experienced by the two men were attributed to the action of fine droplets of H, as they were not typical of contamination with large drops [44].

In 1942 a new way of dispersing H was investigated. Thermal generators had been used for some time to disperse harassing agents such as DA or CN. A trial was conducted in which H was dispersed by a thermal generator [45]. The H thus produced would be in the form of vapour. In determining the characteristics of the generator the following criteria were used [45]:

- H vapour necessary to cause casualties solely from eye effects was assumed to be 100 mg.min/m³;
- to produce casualties by the effect on sensitive areas of the body with warm skin, about 350 mg.min/m³;
- to produce casualties by effects on the skin, where the skin was cool, a minimum of 700 mg.min/m³.

Two field trials were conducted with H dispersed by thermal generators [45].

- In the first trial, three men in normal battledress and wearing respirators were exposed to H at a level estimated to be 500 mg.min/m³. The men continued to wear the clothes worn during the trial for 4 hours afterwards, during which time

they walked about and remained in the open. All three men "became severe casualties necessitating hospital treatment but the full effects did not develop until nearly a week after exposure" [45]. The effects were noted as being much more severe than expected.

- In the second trial, men were exposed to H at concentrations from 190-360 mg.min/m³. Some of the men wore impregnated battledress. Again, the men continued to wear the clothes for four hours after the trial. No effects of military significance were observed. Those men who wore unimpregnated battledress exhibited, at most, only "slight effects".

Two field trials were conducted with H weapons designed to assess the dissemination capabilities of two methods of releasing mustard using volunteers as detectors. The first was carried out in January 1942 [46] and considered a 25 pound artillery shell charged with thickened H. The shells were fired from a range of 400 yards at a screen suspended 100 feet above the ground by a gallows. Before any of the shells were fired, estimations were made of where the drops of H produced by the impact of the shell with the screen would fall and volunteers were positioned in areas where different drop sizes were expected. The 19 men who took part wore steel helmets, skeleton web equipment and eyeshields. The men were in position when the shells were fired at the screen.

After each shell was fired, every man was inspected and firings were "repeated until all men were suitably contaminated" [46]. At that point, each man performed the personal decontamination drill, then half of the men spent the afternoon sitting in a warm room and the remainder went on a route march. The men continued to wear their clothing for 4 hours after the trial. Eleven of the 19 men became casualties and the medical report written about them made the following points [32].

- The trial was carried out in such a way that "when a man had been contaminated sufficiently from one shell as to be considered a potential casualty, he left the target area".
- When the clothing was removed four hours after contamination, there were no subjective symptoms but blisters developed at various sites of the body: neck, shoulder, arm, thigh, knee, elbow, eyelid (by H being transferred there by hand), chin and buttock.
- The 11 men who sustained burns of casualty severity through their clothing were treated at Porton, not being allowed to return to their unit until it was considered that they were fit to be treated by their regimental medical officer and to be able to perform light duties.
- Eight of the eleven men were unfit for duty for 30 or 32 days after the trial. One was unfit for 14 days, and one for 4 days. The report does not say how long the eleventh man was unfit for duty.

The suggestion that a minimum level of contamination of volunteers (perhaps sufficient to render them "potential casualties") was being aimed at in this trial is quite strong. It is reinforced by a later report which noted that because the weather was cold when the January 1942 trial was done, a heavy contamination of the volunteers was "found to be necessary to ensure casualties" [47].

Another trial with H was conducted later in 1942. The report of the trial notes that the volunteers who took part in it were "contaminated to a degree at least as great as demanded by the standard minimum assessment" [47]. It is not clear how this *standard minimum assessment* (SMA) was arrived at but it defined the level of contamination for particular drop sizes of H. For example, for drops of 1.09-1.44 mm diameter, the SMA required a density of contamination of H of 0.15 g per square metre. The conduct of the trial, which was a repeat of the January trial but with men wearing German uniforms and British eyeshields, is outlined below [47].

- The procedure for firing the shells at the screen and the positioning of volunteers (in areas which were expected to be contaminated with different drop sizes) was the same as the January trial.
- Twenty men took part. After each shell was fired each man did 5 press-ups on bare hands, resting the body on the ground for 10 seconds between each press-up ("to simulate the actions which might occur if the men were forced to lie on contaminated ground") and fired 10 rounds from his rifle. After a period of 10 minutes "to allow any contamination picked up to take effect", each man decontaminated his hands. The men were inspected between firings to determine if they were contaminated to the required degree.
- Firings continued and men were removed if they "were considered to be satisfactorily contaminated". The trial was completed by lunchtime, at which point the men went to a dining room and in the afternoon some remained in a warm room while others went on a route march. All the men continued to wear their contaminated clothing during the night. Two men were admitted to hospital the next morning, the remaining men continued to wear the clothing for a further 24 hours (42 hours in all).

Seven of the men are noted in the report as having received at least the contamination stipulated by the SMA (some men received 4, 8 and 13.5 times the SMA) and four of these were deemed casualties after a clinical examination. Two of the four were "sufficiently severely burnt as to require immediate admission to hospital" [47]; one was admitted to hospital 5 days later, solely as a result of burns sustained to the scrotal region. The remaining man was a "borderline casualty" [47]. The report concluded that a German infantryman contaminated with about 4 times the SMA stood an even chance of becoming a casualty.

As mentioned previously (and covered in Chapter 20), a Porton report refers to 31 H casualties being treated at Porton. It would seem that these casualties were volunteers who took part in the field trials just described, some of the H studies outlined earlier in this chapter, and the work (explained in Chapter 20) to investigate the effects of H vapour on the scrotal region.

17.4.2. Harassing agent weapons

Some field trials were conducted with harassing agent dispersed as spray from aircraft flying at low altitudes. A series of field trials was carried out in August and September 1940 [48], each trial considering a different harassing agent: KSK, BBC, CN, DC, bromoacetone, Heilbron 1 and Heilbron 2. The last two may have been German harassing agents. Each agent was sprayed from an aircraft flying at 250 feet. The spray consisted of 10% of the agent and 90% of an innocuous substance, with the exception of the DC spray half of which was DC.

Volunteers, wearing battle dress and eyeshields, and clothed dummies were positioned in the area into which the spray was expected to fall. After the spray had fallen, the volunteers continued to wear their contaminated clothing. The clothing on the dummies was worn by other volunteers.

The density of the spray on the ground was generally about 0.3-1.3 g per square metre, but 2.5 g per square metre in the DC trial. Only slight effects were experienced by the volunteers who took part. BBC induced the most severe effects but only when the respirator was donned after the spray had fallen, thus enclosing in the small volume of the mask the vapour given off by the droplets which had fallen on the face¹ [48]. The report concluded that none of the harassing agents delivered from aircraft as spray appeared promising.

¹ This trial took place before the work with respirators and cellophane outlined in a previous section, and may have motivated the work.

A similar trial was carried out in 1941 with BBC sprayed from a Lysander aircraft over the chemical warfare ranges at Brendon Common, four miles southwest of Lynton [49]. A total of 210 volunteers participated and were placed at various points on the range on which the spray was expected to fall. Each man wore an eyeshield during the spraying and while the spray was falling to the ground. In the event only about a third of the men were hit by spray and very few found it necessary to don their respirators. Some men found walking over the contaminated ground uncomfortable but by no means intolerable. The maximum density at the points occupied by the volunteers was found to be 0.027 g per square metre. The report reiterated the conclusion made earlier: that spraying harassing agents from aircraft did not appear very promising.

A series of trials was conducted with small ammunition containing harassing agents. In August 1941 a trial was conducted at Woolwich to test the armour-piercing qualities and harassing properties of German 7.92 mm armour-piercing bullets which had 23 mg of CN housed in a recess at the base of the core [50]. The conduct of the trial is outlined below [50].

- Only six rounds were available for testing. They were fired from a range of 100 yards at armour plates of different thickness erected in front of the square hatchway in the side of a hull of a scout car. As soon as possible after firing, samples were taken of the atmosphere inside the scout car.
- The atmosphere inside the scout car was tested by volunteers who breathed it from tubes connected to their respirators which ran to the inside of the car. "Owing to the need for personnel to be under cover during the firing of the bullets, a period of at least 10 seconds elapsed before the atmosphere in the vehicle could be tested" [50].
- The mean concentration of CN inside the scout car varied from 0.8-1.3 mg/m³, depending on the thickness of the armour plates through which the bullets were fired. Volunteers experienced lachrymation and some nose irritation.

The report concluded that 23 mg of CN should have produced immediately intolerable effects but that the sampling of the atmosphere was delayed for safety reasons: "considerations of safety to personnel in these trials did not permit breathing tests being carried out at the instant of penetration by the bullets". In other words, because the ammunition was expected to penetrate into the vehicle (thus releasing shards of metal) it was not safe to put observers inside.

Further tests with this German ammunition were conducted in April 1942 [51]. Rounds were fired at armour plates and samples taken of the cloud of CN in front and behind the plate. High speed photography was taken of the passage of a bullet through plate. One round was fired at an Armoured Fighting Vehicle and the atmosphere inside sampled. One test involved a volunteer; details are given below [51].

- To begin with, rounds were fired inside the chamber and the concentration measured by chemical samplers. The concentration varied from about 8 mg/m³, one second after firing, to 7 mg/m³, 30 seconds after firing.
- The facepiece of a service respirator was connected to the top of the chamber. A round was fired inside the chamber (while the volunteer was under cover) and 15 seconds later the volunteer began to inhale the atmosphere via the facepiece, which he continued to wear for 2 minutes. The volunteer experienced lachrymation 15 seconds after donning the respirator but at no time was the effect such as to prevent clear vision and the amount of disability was negligible.

Some trials featured harassing agent ammunition which was not expected to penetrate armour. Trials of this type were conducted in January 1942 [52], and involved "bursterless" grenades (made of glass) containing CN being used against a Valentine tank.

- In the first trial grenades were attached to the side of the tank, which was stationary and closed down for action. The grenades were exploded remotely (by electronic means) and the tank was then opened to see if any of the CN smoke from the grenade had penetrated through orifices.
- After this trial, a grenade was exploded on the front deck of a tank, just below the gun mantle. A volunteer (protected by a respirator) was inside the tank and he attempted to mark the main points of entry of the smoke.
- The next trial involved the Valentine tank, closed down for action and travelling at normal speed, being ambushed by four men throwing glass grenades at it. The driver of the tank wore a respirator and was accompanied by two unprotected observers. When the glass grenades shattered against the tank a cloud of CN dust was formed. Within two seconds of impact, the cloud had entered the tank and induced effects on the observers. The men left the tank but severe lachrymation occurred within a minute of the ambush and continued for 5-10 minutes. CN also entered the driver's compartment. The trial was repeated with the tank stationary and the engine off. No effects were observed in the men positioned inside the tank.

The report concluded that the cloud of CN was drawn into the tank through the forced ventilation system which was active whenever the engine was running [52]. When the engine was off, the cloud of CN was unable to penetrate the tank.

Trials involving ammunition in these circumstances were deemed safe as it was not expected that the ammunition (in this case glass grenades) would penetrate the tank, or damage it to the extent that shards of metal would be released inside the tank. However, a fatal accident did occur during a trial carried out on 3 January 1944 involving three 20 mm bullets containing a small amount of DA [53] being fired at a tank. The bullets were not armour piercing [54]. Eight Service volunteers and a member of Porton staff were positioned in the tank, wearing respirators and eyeshields to ascertain whether any of the DA penetrated the various compartments of the tank [54]. One of the Service volunteers in the tank, sitting opposite the staff member, died from an injury sustained in the trial. One of the bullets discharged a small fragment which penetrated the complicated armour defences of the tank and struck the volunteer in the neck. After a court of enquiry the coroner issued a verdict of death by misadventure [54].

Trials of ammunition fired against tanks and other fighting vehicles recommenced in the late 1940s and early 1950s when nerve agent weapons were being developed. None of these trials involved volunteers. The concentration of nerve agent released by weapons inside the tank was measured by chemical samplers and the effects of the concentrations (if assessed at all) was examined by placing small animals in cages inside the vehicle.

17.5. Miscellaneous work

17.5.1. Studies with nervous system stimulants

A small study was carried out in 1941 with Doryl and an allied substance referred to as T1088. Doryl, the trade name for carbamylcholine chloride, was known to stimulate the parasympathetic nervous system causing salivation, sweating and constriction of the bronchi [55]. Both Doryl and T1088 had been investigated by a professor at Sheffield and open source reports contained details of their toxicity to man.

Two volunteers took part in the study and were exposed at levels of 25 mg.min/m³ and 100 mg.min/m³. The lower exposure level induced no effects. The higher level induced coughing and a fall of blood pressure of 20 mm Hg. The pulse of one of the volunteers rose from 70 to 82 beats per minute and his breathing rate increased. However, the report noted that it was difficult to achieve even the lowest concentration in the field and so neither substance was considered a promising agent [55].

The harassing effects of two fluorophosphates were studied in 1942 [56]. Alkyl fluorophosphates had been previously reported as producing acute contraction of the pupil and a disturbance of visual accommodation and it was felt they might be useful as harassing agents, particularly at night [56]. The rangefinder task was used to measure the impact on performance and was conducted in daylight and in simulated daylight. Di-isopropyl fluorophosphate (DIF) and di-ethyl fluorophosphate (DEF) were used. An outline of the tests is given below [56].

- Twelve volunteers were exposed to DEF at $278 \text{ mg}\cdot\text{min}/\text{m}^3$ ($t = 2$ minutes). All felt irritation of the throat after 10-30 seconds and then tightness of the chest. Within an hour of the exposure pupils had decreased in size by "about 1 mm on average". No significant alteration was observed in visual acuity.
- Twelve volunteers were exposed to DIF at $328 \text{ mg}\cdot\text{min}/\text{m}^3$ ($t = 2$ minutes). By 3 hours after the exposure pupils had become almost pin point size and reflexes to light and accommodation "were lost". The volunteers complained of headache just above or behind their eyes and were unable to sleep during the ensuing night. A day after exposure distant visual acuity was returning to normal but near vision was found to have deteriorated further. "Intensive treatments with 1% homatropine drops in the eye was begun", with one drop being applied in each eye every 15 minutes for 1 hour. The pupils of the volunteers returned to their normal size in 5-6 days.
- Six volunteers were exposed to DIF at $41 \text{ mg}\cdot\text{min}/\text{m}^3$ ($t = 5$ minutes). All complained of tightness of the chest and irritation in the throat. Three hours after the exposure the pupils of the men were only slightly contracted and pupil reflexes were normal. No headache was experienced.
- Eighteen volunteers were exposed to DIF at $99 \text{ mg}\cdot\text{min}/\text{m}^3$ ($t = 3$ minutes). Four to six hours after the exposure pupils had contracted to the size of pin points and headaches developed 18-24 hours after exposure. The volunteers were split into three groups of six: one group received no treatment, one group had 1% atropine sulphate drops instilled in their eyes once, and the final group had a course of 1% homatropine drops over 5 hours. The atropine sulphate drops were found to be best. After this investigation all the men were treated with atropine sulphate drops.

The report concluded that DIF at $99 \text{ mg}\cdot\text{min}/\text{m}^3$ might, if used at night, produce visual harassment but this was a high concentration to achieve in the field and so "the value of alkyl fluorophosphates as chemical warfare agents is extremely doubtful" [56].

17.5.2. An H trial on a railway

One instance has been found of Porton conducting a trial with a chemical warfare agent on public ground involving civilians [57]. The work was prompted by concerns over repairing damaged railways after enemy air raids. To minimise disruption, damage to railways had to be repaired quickly. If the enemy used bombs containing H (mustard gas), as well as high explosive bombs, the repairs might be slowed down. To investigate the extra effort to repair a damaged railway with H contamination and to identify the correct procedures to be adopted, Porton conducted a test on a disused loop line near Medbourne in Leicestershire. The conduct of the trial is described below [57].

- A crater was blown in the railway line and the following morning the crater and surrounding spoil thrown up by the explosion were contaminated with H by detonating two chemical mines. The mines discharged a total of 8 gallons of liquid H.
- The crater was about 30 feet in diameter. "Unfortunately on the day of the trial, the wind blew across the railway line and at the time when the contamination was

laid, the breeze was strong with driving rain". "Some contamination was therefore carried into the neighbouring field and it was deemed advisable to warn the owner not to turn cattle into it for a few days."

- About 2 hours after the contamination (a delay which would in practice be a minimum) LMS Railways repair gangs came to the scene and started work. About 60 men were employed and they were told that H had contaminated the scene. No decontamination was carried out before the gangs arrived or while they were repairing the line.
- The LMS Railway repair gangs wore impregnated suits provided by Porton which conferred complete protection against the H vapour on the body. The men wore the standard outfits issued by the LMS for this kind of situation: steel helmet, civilian duty respirator, long oilskin coat, oilskin gloves and rubber boots.
- Each man wore detector papers and in only three cases did vapour from the H contamination induce a definite reaction in the paper (all these cases featured paper attached to the legs). The concentration of H vapour was measured and found to vary, between 1.5 -4.5 mg/m³ depending on distance from contamination source and time after contamination.

Repair work was slower than normal. Many of the men "were above military age" and found only short periods of work possible in the protective clothing they were wearing. The absence of an organised procedure to prevent an avoidable spread of contamination on tools, railway track and clothing led "to complication and definite danger". None of the men experienced any effects of H. The points made by the report were as follows [57]:

- the men (civilians without gas training) had an exaggerated view of the danger of H and some precautions were overly elaborate but, on the other hand, some obvious precautions to avoid spreading the contamination were omitted;
- a Gas Safety officer should inspect sites of bomb damage before repair workers arrive and should remain on site while repairs are being effected;
- the clothes of the repairmen should be left where they bathe and kept away from the contaminated site;
- contaminated outer clothing and boots should not be worn in closed vehicles (for example, vehicles used to transport repairmen from the site to the bathing area).

It is not known if these points were taken up by the LMS or promulgated within government departments.

Chapter 18. Other chemical warfare agent studies after 1945

18.1. Human studies with H

18.1.1. Introduction

Human studies with H continued after World War II. Most concerned treatment or protection and are described in Chapter 20. Generally they took one of two forms. First, a drop of H would be placed on the bare skin (usually the arm) and then a method of decontamination would be tried. These methods of decontamination included mechanical ones (swabbing, dabbing and so on) or the application of an ointment, powder or cream. Second, fabrics and materials which were being considered for incorporation into future protective clothing would be subject to an "H penetration" test. A piece of the fabric under test would be attached to the bare skin of the arm (sometimes a few pieces of different fabrics might be attached in layers) and then a few drops of H liquid would be applied onto the fabric. The test assessed whether the fabric prevented H penetrating to the skin.

Although these two forms of study are described in Chapter 20, they are summarised here partly for context and partly because H penetration tests played a part in the cessation of human studies with H at Porton. The details of that will be recounted in this chapter. Also contained here are those human studies with H conducted after World War II which were not conducted specifically to test a treatment or protective fabric. They include some further work on H sensitivity studies and two short miscellaneous tests, one of which included L.

It should be noted that H was regarded as a threat throughout the period covered by the survey. Even after the advent of nerve gases, the CDAB considered H in 1954 to be an important CW agent, which was cheap to make and known to be held in large quantities by potential enemies [1]. H continued to be regarded as a threat into the early 1970s, when a review of treatments for mustard gas injuries was started [2], and in 1979 was held to be one of the most potent and militarily useful chemical warfare agents [3]. H remains one of the chemical warfare agents regarded as a threat to the UK Armed Forces.

18.1.2. H sensitivity studies

The standard H sensitivity test (where a drop of H of 1 in 10,000 was applied to the arm of a volunteer) which was used from the early 1930s to screen out sensitive men from H studies, continued to be used after the war. Three studies were carried out in the immediate post-war years to improve the understanding of the effect of H on skin. The first assessed the effect of repeated application of drops onto the same skin site. The second looked at how skin reaction varied according to the concentration of H in the drop and the third compared the skin reaction to H at different places in the body. No report has been found of these studies; the details are drawn from experimental records.

The investigation of the effect of the repeated application of H was separated into two parts and they are described below.

- In December 1945 "successive drops [of H] directly over the previous drop immediately on drying" were applied to a site on each shoulder of 4 volunteers [4]. Five drops in succession were applied to each shoulder and the resulting skin reaction monitored over the course of the following 4 days. The concentration of H in the drops used varied from 1 in 50 to 1 in 500. The same four volunteers subsequently had successive drops of 1 in 500 H applied on a site on their right deltoids. The experimental record does not make clear how many drops were applied in succession but the table therein refers to up to 12 drops [4].
- The second part of the repeated application study was conducted in January 1946 [4]. Successive drops of H (of 1 in 100) were applied to one armpit of each of 14 volunteers. One drop was applied, followed by another when the first had

dried, then two more drops 6 hours later with a final 2 drops 18 hours after those [4].

Tests of the skin reaction to different concentrations of H drop were conducted during 1946 [4]. Typically, drop concentrations of 1 in 100, 1 in 500, 1 in 1000 and 1 in 5000 were used, each volunteer who took part having a single drop of each concentration applied to a different site on his deltoid. Around 75 volunteers participated in this test [4]. There were some variations in this procedure, described below

- Two men in January 1946 had five drops, instead of four, and of different concentrations applied (1 in 17, 1 in 21, 1 in 31, 1 in 62 and 1 in 125); five men had concentrations 1 in 31, 1 in 62, 1 in 125 and 1 in 500; a further three men had 1 in 10, 1 in 17, 1 in 21 and 1 in 31.
- 46 men in 1948 had only three drops (1 in 500, 1 in 1000, and 1 in 5000) applied;
- Seven men had "saturated H vapour" directed against a site on their arm for 6 minutes four times, although it is not clear from the experimental record if the same site was used on each of the 4 occasions.

The third H study in April 1946 compared the reaction to H of different body sites [4]. Three volunteers took part. Each had four drops of H, of the same concentrations as the previous study (1 in 100, 1 in 500, 1 in 1000, and 1 in 5000) applied within a 4 cm square area on 10 sites on their body. The sites used were the neck, chest, armpits, deltoid, the fold of the elbow, inner thigh, middle thigh, the gluteal fold, and the back of the knee.

18.1.3. Short miscellaneous studies with H, HT and L

Two miscellaneous tests were conducted. In June 1948, seven volunteers took part in a "demonstration of H or L blisters for MDG and MD/RAF" (two senior visitors from the Army and RAF) [4]. The volunteers had one 1.1 mm diameter drop of L and one 0.5 mm diameter drop of H applied to each arm. The two drops on their left arm were treated with ointments; the two on their right arm remained untreated. The experimental record does not indicate how long before the two senior visitors inspected the arms the drops were applied.

The second short study was prompted by RN interest in the hazard arising if men touched greasy surfaces which had been contaminated with mustard gas [5]. The work was carried out in January and February 1968 [6] and used drops of HT, a mixture of H and Di-(β -chloroethylthio)-diethyl ether (T) in the ratio 60% H and 40% T [7]. Different drops of HT were applied between the wrist and elbow [4]:

- two volunteers had three drops of 10, 20 and 30 mg of HT;
- two volunteers had two drops of 100 μ g of HT;
- two men had three 100 μ g HT drops and two 400 μ g drops of 25% HT in naval grease;
- one man had two 100 μ g HT drops and one 400 μ g drop of 25% HT in naval grease;
- five men had five 100 μ g HT drops, three of which were applied over grease.

The experimental record does not stipulate how long these drops were left in place, nor why HT was used. The COSHE, in considering the proposed study in 1967, stipulated that drops should be left in place for a maximum of 30 minutes [5].

18.1.4. The cessation of H studies

The details of the cessation of H studies at Porton start with a request in 1977 [8] from the DNBBCC for Porton's advice on the H "confidence test", then in use in chemical warfare training. The test (described also in Chapter 7, Section 7.2.2) involved a drop of H being placed on the skin which was then immediately treated with the personal decontamination procedure then in force. The test was aimed to give confidence that the decontamination procedure worked. The DNBBCC, in approaching Porton for advice in September 1977, was considering changing the nature of the confidence test in light of concern over the repeated exposure to H and made the following points about the test [9]:

- sometimes members of the Services undergoing training were asked if they would volunteer for a "delayed decontamination confidence test" (in which up to 10 minutes was allowed to elapse between the application of the drop and decontamination [10]) or to grow blisters;
- if a man had grown a blister during training, they were not allowed to volunteer to do so again, nor if they had undergone the usual confidence test within the previous 12 months;
- no-one was allowed to volunteer for two delayed decontamination tests.

COSHE considered the request in October 1977 [9] noting that "available evidence suggested an increased risk of cancer in those repeatedly exposed to large inhalation doses of mustard. The danger of cutaneous [skin] burns was unclear and it was very unlikely that a single exposure to a small quantity was of any consequence" [10]. COSHE decided to consult a specialist at the Royal Cancer Hospital before coming to a view about the H confidence test.

The consultation resulted in a meeting between the specialist and representatives from Porton and the DNBBCC in January 1978 [11], which came to the following conclusions:

- the evidence from animal experiments involving repeated exposure to H is "overwhelming that H is carcinogenic under the conditions of the animal tests";
- epidemiological evidence "strongly suggests" an association between repeated exposures of man to H and subsequent development of "malignant neoplasms";
- no evidence from either animal experiments or epidemiological surveys suggested that single exposures to H are "likely to be conducive to" the subsequent development of neoplasms;
- although single exposures of H are unlikely to cause long-term adverse effects, the practice of using a known carcinogen for a confidence test (and for which a simulant might be made available) is to be regarded as a procedure for which the support of CDE [Porton] cannot be recommended;
- the practice of instructors at the DNBBCC exposing themselves to H several times a year should be "strongly discouraged".

By March 1978 Porton had formed a clear view that the confidence test used in chemical warfare training should be banned but that this ban should not extend to the use of H at Porton [12]. At that time H was used with humans only for the H penetration test. The differences cited by Porton were as follows:

- volunteers were only used once for such tests [12], even if they attended Porton as volunteers on more than one occasion [10];
- any effects on the skin if H penetrated the fabric were "not induced intentionally".

It was noted that the volunteers who took part in H penetration tests "were always told of a slight risk of receiving a burn if the clothing was defective" but "it appeared irrelevant to warn them of mutagenic hazards" [12] as giving information "... on a non-existent risk ... could only generate unnecessary alarm." It was added that "... a medical officer should, of course, always be prepared to give the information when asked" [13]. COSHE was not sure that an H simulant suitable for penetration work was available and, if H was abandoned, the work on protective clothing would be "seriously affected" [13].

In May 1978 COSHE discussed the use of H in penetration tests at Porton in light of unexpected incidences of erythema and vesication in volunteers involved in a H penetration test of new aircrew over-garments [14]: no effect had been expected. Further, there was evidence of volunteers having received burns from H penetration tests when they returned to Porton some months after the test had been carried out [14]. COSHE suggested a suspension of H penetration tests at Porton in May 1978, until advice had been taken [14].

By July 1978 consideration had been given to the consequences of stopping H penetration tests and the effects on the programme of work with protective clothing [15]; simulants for H for penetration work were investigated over the summer [16]. The matter was considered by the MC in 1979.

Some time previously the MC had learned of an epidemiological study of UK ICI workers who had been employed in the manufacture of H in Merseyside [3]. In 1979 the MC was given advanced sight of the preliminary findings [17], which are summarised below, together with an outline of the nature of the study.

- The study attempted to trace the 502 British workers (359 men and 143 women) who had worked on the manufacture of mustard gas during World War II. Up to the end of 1974, the study had managed to trace 419: 181 had died since the war, 6 had emigrated and 232 were still alive.
- The number of deaths, from all neoplasms combined and from all other causes, of the 181 workers who had died since the war was not significantly different from the numbers expected from national death rates.
- However, three workers had died of cancer of the larynx and one from cancer of the trachea, where the expected number of deaths from this causes is 0.4. Further, seven workers had cancer of the larynx, against an expected number of 0.75.
- The excess of cases of laryngeal cancer was highly statistically significant even with the conservative assumption that all the untraced workers were still alive. All but one of the cancers among the group of workers was diagnosed more than 20 years after the end of World War II.
- The excess of laryngeal cancer among these workers accorded with previous observations made in Japan.

The MC considered these findings in October 1979 [18]. At that time human exposures to H at Porton were still in abeyance. Porton explained to the MC that only single exposures to H had been permitted for any volunteer over the past 20 years and asked if the MC knew of any "one-shot" carcinogens. The MC concluded that, at that time, the evidence for long-term hazards arising from single exposure to H was tenuous. However, the MC noted that the epidemiological study would stimulate interest, and possibly more studies, which may change the evidential situation.

No further discussion of the use of H in human studies has been found in subsequent COSHE and MC proceedings. However, after May 1978 no H penetration tests with volunteers are recorded in the experimental records. It appears, therefore, that human studies with H ceased in May 1978.

On a final note, in March 1979 the DNBCC asked Porton for advice on the "sniff test" [19], then in use in chemical warfare training. The sniff test (described in Chapter 7, Section 7.2.2) gave members of the Armed Services an opportunity to become familiar with the characteristic odour of H. Porton replied to the DNBCC in March 1979 [20] stating that, from a medical perspective, the sniff test could be justified if exposures to H were single and limited (in dosage) and that the test might mean the difference between life and death in the field.

Later in 1979 Porton augmented their advice [21] having reviewed the knowledge available on the odour of H. That review suggested different people had different sensitivities which would cause considerable variations in individuals' perception of the nature of the odour of H. The sniff test was, therefore, a highly subjective experience. Further, it was noted that efficient military drill in chemical warfare environments would be possible even if members of the Armed Services did not know what H smelled like. Porton concluded that there appeared no practical reason for keeping the sniff test as part of chemical warfare training.

18.2. Human studies with dye-markers

18.2.1. Introduction

Dyes are not strictly chemical warfare agents. However, they were developed for use in chemical warfare activities, so dye studies are recounted here as opposed to the non-chemical warfare section.

An obvious application of dyes is to serve as a means to mark people involved in riots or internal security incidents. The inclusion of a dye in water cannon and squirts not only serves to quell disturbances but makes possible the identification of marked rioters some time after the event.

Dyes were also developed for other activities: for example, a dye was added to the simulant used for VX in field trials to assess how much agent a man might pick-up from contaminated ground. Dyes were also used for training purposes. Work with fluorescein as a dye in SPAD devices developed for training [22] is described in Chapter 15 (Section 15.3.5). Human studies with dyes in these different areas of chemical warfare are described in the next few sections.

18.2.2. Dye-markers for internal security

The earliest mention of the use of dyes for marking miscreants in internal security problems appears in 1965. A grenade had been developed specifically for marking purposes and possible dyes had been identified for it. COSHE ruled that the dyes should be tested on animals to see if they exerted any harmful systemic effect [23]. Crystal violet dye was subsequently rejected for marker grenades because in rabbits it produced moderately severe and prolonged damage to the eye [24].

Dyes for use in water cannon were investigated with animals in the early 1970s before some were chosen for trials involving Service volunteers. Five dye solutions were approved by COSHE for the trials: astrazone pink and certicol black, astrazone red violet, blancophor 766, blancophor and certicol yellow, and standacol violet [25]. None of these dyes were an irritant to the skin; three of them were standard food additives (certicol black, certicol yellow and standacol violet) and the other three had been found to have LD50 in rabbits of 1.15 to 3.4 g/kg body weight [26].

Each of the dye solutions was to contain Uvitex as a covert marker [27]. Uvitex can be detected by ultra-violet (UV) light and COSHE stipulated that, during the trial, care should be taken when using UV light on the faces of volunteers [26]. Uvitex and other dyes which could be detected by UV light had been tested on the skin of volunteers in February and March 1971 [28]. Thirteen volunteers took part, each having 4 ultra-violet dyes placed on their skin.

The trial for which these dyes were approved took place at the School of Infantry at Warminster in July 1972 [26]. The elements of the trial are described below.

- Each dye was sprayed from a SPAD device onto the upper trunk and face of three volunteers. Each man was instructed to keep his eyes closed during the spraying, which lasted 2 seconds. The volunteers had their hair covered during the spraying.
- The men were then given an hour to wash thoroughly and to use common domestic cleaning materials to remove dye from their clothes. They were given a financial incentive to clean thoroughly [29].
- After washing, the men redressed and mingled with other men who had not been sprayed with dye (but who had showered and washed). Two officers of the School of Infantry then attempted to discern the men who had been marked with a dye solution by a careful visual inspection and the use of UV light.

Astrazone red violet and blancophor 766 were found to be the best dye solutions from this trial [29]. Other trials of dye-marking systems were conducted as follows [30].

- Volunteers were sprayed with dyes and the distance the dye could be observed from, and the effect of washing was determined. Covert dyes (like Uvitex which could be seen only under UV light) were applied to volunteers who then entered a darkened bus to be examined under UV light.
- To find out if dyes could be transferred, a trial was held in which two of four chairs available for the use of volunteers had been marked with dye. Men were inspected to find out if dye had been picked up from the chairs.
- A group of volunteers played ball games for 30 minutes in which considerable personal contact was involved. Before the games half the men had been marked with dyes, the other starting the games free of dye. Some transference was noted.

18.2.3. Dyes for trials at Porton

Dyes were occasionally used in trials at Porton to enable the degree of contamination to be determined. The CR squirt trials recounted in Chapter 15 (Section 15.5.3) used the food additive Standacol Violet for this purpose [31].

Trials to determine the degree to which VX might be picked up from contaminated ground also used dyes. These trials, described in Chapter 9 (Section 9.5), used a simulant for VX, diethyl phthalate (DEP). In the 1950s a series of dyes were tested for DEP with animals, from which Orasol Brilliant Fast Red was chosen [32]. This dye was used with DEP in simulated VX field trials in the late 1950s [33, 34].

From December 1962 to February 1963 alternative dyes were considered for DEP in human studies to test the sensitivity of skin to them [35]. DEP with 4% Brenthal FR and 1% Brenthal FO were tested. The mixture was applied to the upper arm either as powder (50 mg) or solution (10 ml) on lint. The reaction of the skin to Uvitex was considered in some of these tests [35]. Twenty one volunteers took part in the DEP and Uvitex tests. Field trials with dyed DEP were conducted after these tests but the reports do not stipulate which dye was used [36].

18.2.4. Dyes for training purposes

Uvitex had been used as a dye in an exercise at Porton in 1973 [37] to monitor the cross-contamination which occurred during the handling of casualties. The exercise had employed volunteers to act as casualties and members of Field Ambulance units practised protecting

them by using casualty bags made of protective material [38]. Uvitex had been applied to the clothing worn by the volunteers acting as casualties and on the ground around them [37].

In 1975, Exercise Hot Box, a series of trials to examine techniques for handling casualties in a chemical warfare environment was being planned [37]. The use of Uvitex in the 1973 exercise was reviewed. Although the degree of contamination picked up by the medics handling the casualties could be gauged after the event by detecting Uvitex with UV light, it had not been possible to identify when cross-contamination had occurred [37]. Therefore it was proposed to add CR to the Uvitex solution used, thus giving an immediate subjective indication of when the medics became contaminated [37]. As in the 1973 trial, the marking solution (this time with CR) would be applied onto the clothes of people who were acting as casualties and on the ground around where they lay [37].

COSHE stipulated that before making a decision about using CR and Uvitex in Hot Box, work needed to be carried out with animals [37]. This was completed later in 1975 and no adverse effects were observed [39]. Accordingly, COSHE approved the CR and Uvitex mixture for use in Hot Box. As mentioned in Chapter 7 (Section 7.3), Hot Box took place in 1976 with Service volunteers acting as casualties.

A series of tests was conducted from October 1964 to August 1965 [40] into the sensitivity of the skin to a mixture of Dyestuff Q and cyclohexylamine. It is not clear why these tests were carried out but, in parallel, the sensitivity of the skin to a mixture of Dyestuff Q, cyclohexylamine and Fuller's Earth was tested. Fuller's Earth was tested and adopted in the early 1960s as a decontaminant for liquid H from skin (as described in Chapter 20). Therefore it is possible that Dyestuff Q and cyclohexylamine were to be added to Fuller's Earth so it would be possible to determine whether troops had applied Fuller's Earth properly during training exercises. While Dyestuff Q would have left a mark on a man using Fuller's Earth, the part played by cyclohexylamine was unclear.

Under the tests one of the mixtures was placed on the upper arm of a volunteer and the reaction of the skin checked 4 hours and 24 hours later [40]. One hundred volunteers had the mixture of Dyestuff Q and cyclohexylamine applied; 91 volunteers tested the mixture combined with Fuller's Earth. A few of the men had two applications, generally separated by 10 days [40].

The remaining work with dyes which appears in the experimental records is a series of tests to assess the skin reaction to collodian dye in 1972 [41] and 1973 [42]. For the tests carried out in 1972, collodian dye was applied to 6 small areas on each arm, and the skin reaction noted. Thirty four volunteers took part in the 1972 tests and the experimental records show that 3 of them experienced slight erythema [41]. Tests in 1973 ran from January to March, and collodian dye was applied to 3 small areas on each arm. Thirty volunteers participated in the tests in 1973 [42].

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