

**Historical Survey  
of the  
Porton Down Volunteer Programme**

**Executive Summary**

June 2006

# Foreword

*by the Minister for Veterans, Tom Watson MP*

The United Kingdom's chemical warfare research dates back to 1916, when the War Department opened an experimental ground at Porton Down, near Salisbury in Wiltshire. Since the late 1950s the central role of Porton Down has been to ensure that the UK Armed Forces are provided with effective protective measures against the threats posed by chemical and biological weapons. The Porton Down Volunteer Programme has played a key part in this objective and the Ministry of Defence is indebted to the many thousands of Servicemen and, latterly, Servicewomen who have participated in studies. I would like, therefore, to express on behalf of the MOD and all members of the Armed Forces, past and present, deep gratitude to those Servicemen and Servicewomen who have volunteered over the years to take part in trials at Porton Down.

# Introduction to the survey

## Background

On 21 November 2000 Dr Lewis Moonie, then Minister for Veteran's Affairs, announced a package of measures intended to address emerging concerns that some Porton Down Volunteers (PDVs) suffered unusual ill health because of their participation in trials at the Chemical Defence Establishment, Porton Down<sup>1</sup>. The Ministry of Defence (MOD) has seen no scientific evidence to support this belief but takes such suggestions seriously. In May 2001 the Minister, as part of the MOD's commitment to assist former PDVs, announced the intention to publish a Historical Survey of the Porton Down Volunteer programme.

Although members of the Armed Forces (Service volunteers) have taken part in chemical warfare studies at Porton Down since 1916 the survey is limited to the period 1939 to 1989, which is of most interest to volunteers.

## Aims

Our aims in publishing this survey are:

- to give a full description of the size and shape of the studies in which volunteers took part;
- to explore the ethical aspects of the studies including how volunteers were recruited, how the studies were described to volunteers, and whether the consent of the volunteers was obtained. At various times during the period covered by the survey, guidelines and codes were published by national and international bodies about the ethical conduct of human studies. The survey describes how the procedures used at Porton were influenced by these guidelines and codes and how they reflected contemporary practice;
- to complement the information available to volunteers through the Porton Down Helpline, which offers volunteers the opportunity to inspect their own records relating to the trials that they took part in at Porton Down; and
- to give them an appreciation of the wider study programme.

## Scope

There is a distinction between chemical and biological research. This survey is concerned only with research into chemical warfare which was carried out at CDE Porton Down as part of the human volunteer programme<sup>2</sup>. Biological research and development work was also conducted at the Porton Down site but in a unit known from 1957 to 1979 as the Microbiological Research Establishment (MRE)<sup>3</sup>. This was completely separate from the CDE and not covered by its organisation or committee hierarchy. The work of the MRE is not covered by this Survey.

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<sup>1</sup> Throughout the survey report "Porton" is used as a convenient shorthand for the Chemical Defence Establishment (and the many other names used to describe it in the period 1939-1989).

<sup>2</sup> Except where specifically stated all references to trials refer to human studies and not tests involving animals.

<sup>3</sup> From 1940 to 1946 the unit was known as the Biology Department and from 1946-1957 as the Microbiological Research Department.

Information on the human studies conducted at Porton has been extracted from documents<sup>4</sup> and volunteer records. The documents fall into distinct categories.

- **Porton technical reports, notes and memoranda of individual studies.** Generally these were written soon after studies were completed, although some were produced a few years later. They usually describe human studies in detail. Complete sets of these documents, produced between 1939 and 1989, still exist.
- **Porton formal progress reports.** These were produced for senior staff in the Government department under which Porton operated. These documents describe the full gamut of work at Porton, from laboratory explorations to animal and human studies. Sometimes, notably during the Second World War and immediately afterwards, these formal reports were produced quarterly or half-yearly. From the 1960s, they were produced annually. Almost all of these reports still exist.
- **Porton progress statements.** Generally these were produced for the meetings of various committees which reviewed the work done by Porton and gave detailed direction for future studies. These documents give details of human studies.
- **Committee meeting minutes.** Virtually all the minutes of meetings of the committee which oversaw and guided Porton's work still exist. Apart from containing information about studies, they are useful in gauging the importance and validity of the conclusions drawn in Porton technical reports.
- **Working files.** These files cover many subjects of relevance to the survey. Complete lists of the files which existed at one time or another have been found. Few of the files themselves have survived. A few are preserved in the Public Records Office and some are held in MOD archives.

Volunteer records exist at Porton which describe the human studies completed since the 1920s. Generally, these records come in several forms.

- **Alphabetical logs**, which list the name, service number and unit of each volunteer who participated in Porton studies. An almost complete set of these logs for the period covered by the survey still exists.
- **Summary books**, which describe the studies in which each volunteer took part during their time at Porton. No details of the studies are given: they are referred to by single words or acronyms. Virtually a complete set of summary books exists for the period covered by the survey, although some periods in World War II have no summary books.
- **Experimental logs**, giving details of human studies, the chemical warfare agent used, the way it was administered and physiological measurements taken from volunteers before and after the study. Detailed logs exist for studies done up to around the mid-1960s. Thereafter, experimental logs were kept by individuals at Porton responsible for each study, rather than as a central pool of documents.

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<sup>4</sup> References shown in normal type are already in the public domain, lodged in the Public Records Office (PRO) at Kew under the Government's 30-year rule. Those references include the PRO piece number (typically, WO189/1234): the label used to request documents at the PRO. References in bold type are not in the public domain, either because they are less than 30 years old, or because some aspect of them precludes open publication under the 30-year rule. **The MOD will devote no effort (other than required by these procedures) to release these documents, either in whole or in sanitised form, to the public domain.**

None of the experimental logs kept in this way after the mid-1960s has been found by the survey team.

- **Diaries**, which describe the various medical examinations made of volunteers, the studies in which the volunteers took part and any symptoms they experienced. These diaries, which start in the 1960s, do not give full details (as in the experimental logs) of the human studies and sometimes refer to them in vague terms.

The volunteer records and the MOD documents provide a rich source of information on the human studies. By cross-checking between them a fairly complete picture of the human studies emerges. There are, however, some uncertainties. Experimental logs covering part of 1963 and 1964 are missing. It is possible, from other documents which have survived and cover this period, to piece together the nature of the human studies done in this period, but some details are lacking about the precise doses and agents used in some of these studies. These uncertainties are evident in the description of the programme of studies into incapacitating agents, and are described fully in the main text.

Formal technical reports were not produced for every human study completed at Porton, nor was every human exposure reported to the various committees (although the committees often discussed studies for which no formal report has been found). For that reason the volunteer records are vital for a complete picture to be painted. From cross-checking the records, it would appear they have been maintained diligently from the point of view of recording the nature of the human studies, in the sense that no reference has been found in reports or committee minutes to studies which do not appear in the existing volunteer records.

In summary, the survey team is confident that the description of the human studies in this report is complete, albeit with some uncertainties on the incapacitating agent programme which are explained in the text.

## **The Executive Summary**

This summary provides a broad outline of the areas detailed in the main historical survey. It provides a general background to Porton's work and the PDV programme and outlines the contemporary ethical standards against the background of which the research programme was conducted. Throughout the summary footnotes direct the reader to the appropriate parts of the main Historical Survey.

The survey has been conducted by MOD officials who had no previous professional contact with Porton. No member of Porton staff was involved in determining the ground the survey should cover or the documents which were to be consulted. Porton's advice has been sought in order to clarify explanations of scientific matters (for example, the effect of agents and treatments on physiology and the metrics used to measure doses and exposures). They have not had any further editorial involvement.

With the exception of the following parts, the survey was conducted by MOD officials. The commentary on codes and guidelines on the ethics of research, and how they were implemented in practice (Chapter 22), was conducted by Dr Alasdair Maclean, Senior Lecturer in Law at the University of Dundee. The commentary was produced independently of the MOD, which exerted no editorial control over Dr Maclean's commentary. Dr Maclean was not told until after he completed the commentary that the survey covered chemical warfare trials conducted at Porton Down. At the outset Dr Maclean was told only that the MOD wished to have a commentary on the development and practice of ethics relating to research with healthy adult volunteers over the period 1939 -1989. The second part of the

survey, which was conducted independently of the MOD by Sir Ian Kennedy, Emeritus Professor of Health Law, Ethics and Policy, concerns an ethical assessment of Porton's conduct (Chapter 23). Sir Ian completed this assessment after the remainder of the survey was completed. The MOD had no editorial control over the assessment: what appears in it was determined solely by Sir Ian. The remainder of the survey was researched and written by MOD officials, although Sir Ian Kennedy has supervised the work, reviewing all drafts, identifying areas which needed closer attention and suggesting methods of analysis and presentation.

## Volunteers

The people who took part in these studies were predominantly Service volunteers, although members of staff at Porton also participated. The history of volunteers being recruited from the Services dates back to 1925, with the introduction of what was known as the "observer scheme"<sup>5</sup>. Under this scheme volunteers attended Porton for a period of 1-4 weeks, during which time they were likely to have participated in many different studies.

Service volunteers were paid according to the number of tests they underwent<sup>6</sup>. Generally, over the period covered by the survey, the payment a regular Service volunteer received for a week's stay at Porton was about half his weekly pay. For National Servicemen, who were paid less than regulars, the payment received at Porton was roughly equivalent to their weekly pay. All Service volunteers who attended Porton remained on duty and, hence, continued to receive their military pay in addition.

## Recruitment

Originally volunteers under the observer scheme were sought through recruitment notices displayed at military units. Before 1964 these notices were drafted either by the Service to which the unit belonged, or by someone at the unit<sup>7</sup>. Despite comprehensive searches of MOD central archives and a search request to all Service units worldwide very few notices used before 1964 have been found. The earliest notice found was used in November 1958<sup>8</sup>, although documents discussing the wording to be used in notices before 1964 have been discovered. From 1964, recruitment notices appeared in official Service and joint Service administration instructions, most of which still exist. A film was made in 1965 explaining the work of volunteers at Porton<sup>9</sup>. The film was available at military units for Service personnel to watch if they wished.

Very often the observer scheme failed to produce enough volunteers for the work that Porton was required to do. Various schemes were considered to increase the number of Service volunteers provided by the observer scheme: arrangements were made for members of the British Army on the Rhine to volunteer, and Servicewomen were allowed to volunteer from the mid-1970s<sup>10</sup>. Various ways of augmenting the observer scheme were introduced<sup>11</sup>, and resulted in Service volunteers being sought for specific studies (rather than to attend Porton for a specific period of time) through a system known as *special intakes* introduced during the 1960s. Special intakes were sought through military authorities sending out signals to units<sup>12</sup> although unfortunately none of the signals used have been found. Some human studies, most notably into the effect of treatments, were conducted with volunteers whilst they remained at their own units.

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<sup>5</sup> Chapter 5, Section 5.1

<sup>6</sup> Chapter 5, Section 5.5

<sup>7</sup> Chapter 21, Section 21.1

<sup>8</sup> Chapter 21, Section 21.2

<sup>9</sup> Annex I

<sup>10</sup> Chapter 5, Section 5.2

<sup>11</sup> Chapter 5, Section 5.3

<sup>12</sup> Chapter 21, Section 21.3

Consideration was given at various times from the 1950s onwards to augmenting the volunteer pool by seeking civilian volunteers<sup>13</sup>. For various reasons, this move was rejected. The only civilians who took part in human studies at Porton were volunteers from the Porton staff.

The number of Service volunteers attending Porton during the period covered by the survey<sup>14</sup> is summarised at Table 1.

**Table 1 - Porton Down Volunteer Programme - Attendance Numbers**

Period	No. of Service volunteers attending Porton
1939-1948	8691
1949-1958	6154
1959-1968	2729
1969-1978	2280
1979-1989	1898

## Information given on recruitment

Those notices found by the survey used before 1964 generally give very little information about the studies for which volunteers were sought. "Physiological tests" is a phrase commonly used. The description of risk and discomfort in notices in this period seems to have varied. For example a notice used in 1950 explained that "there was not the slightest element of danger" in the tests. In 1953, after the death of a volunteer following a nerve agent study, the Treasury Solicitor suggested this should be amended to "[tests] are arranged so as to eliminate foreseeable danger". This phraseology seems to have been adopted by some of the Services in their notices, but the words are not used in Royal Navy notices from 1958 to 1963, which employed phrases akin to "the physical discomfort resulting from them [the studies] is usually very slight".

MOD documents from 1959 and 1961 clearly show that statements about physical discomfort and danger were intentionally omitted from later notices so as not to deter volunteers from coming forward. Notices during the period 1962-63 read "[The studies] result in little or no discomfort", although some notices during this period explained that volunteers had the right to withdraw from any study.

Notices used from 1964 continued to vary in their description of the risk associated with studies, but went further than before. Some notices from 1964 and into the mid- to late-1970s stated that "there is no danger to the individual", while others in the early 1970s noted that the "tests are neither unpleasant nor severe." The right to withdraw from studies, and to refuse to take part in particular ones, was more frequently mentioned in notices from 1964. From the mid-1970s more was often said about the nature of the studies for which volunteers were sought.

## Information given on arrival

Details of the information given to volunteers while they were at Porton are occasionally found in MOD documents. Civilian volunteers were being considered in 1961, and prompted Porton to write a paper on the arrangements in place for Service volunteers and how they

<sup>13</sup> Chapter 5, Section 5.4

<sup>14</sup> Chapter 5, Section 5.6

might be applied to civilians. The paper described the information given to Service volunteers, and the explanation of their right to refuse to participate in studies.

Naturally the volunteers and ex-members of Porton staff should serve as a rich source of historical information; however, contact with these people was constrained<sup>15</sup> for the following reasons:

- The Data Protection Act 1998.
- The Wiltshire Constabulary's criminal investigation. Advice from both the Wiltshire Police and the MOD Legal Advisor had prohibited contact with ex-members of staff while the criminal prosecutions remained a prospect. At the time of drafting, the Crown Prosecution Service was considering cases against former members of staff.

Only the 600 or so volunteers contacted by the police have been canvassed by the survey. Some 400 of them kindly completed a questionnaire, but the sample of 400 is small compared to the total number of volunteers who attended Porton over the period covered by the survey.

Some of the volunteers who have contacted the Porton Helpline have commented on what they remember about their time at Porton, and these comments have been used by the survey, although the Helpline staff did not specifically seek them. Some ex-Servicemen who attended Porton as volunteers report that they believed they would be taking part in research relating to the common cold. Porton Down did not undertake research into the common cold and neither the survey team, MOD Historical branch nor the Wiltshire Police have found any evidence linking it, either through recruitment notices and films, or other official documentation, with cold research.

From 1964-1977 volunteers who attended Porton were interviewed when they first arrived. The interviewer sought personal information (family history, Service career, habits etc.) from the volunteers and also asked why they had volunteered. The answers given were recorded on a card. Of the 2250 volunteers whose card still exists only 5 mentioned the common cold as a reason for volunteering. That contrasts with the questionnaire responses of the 77 volunteers who attended Porton from 1964-1977, 14 of whom wrote that they thought they were going to Porton for common cold research.

According to a Porton document produced in 1961, "volunteers are briefed on their first morning [at Porton] as to what will happen to them and given the chance to withdraw"<sup>16</sup>. No other MOD documents have been found which give any more information about the nature of this initial briefing, although the recruitment film of 1965 mentions volunteers' right to withdraw from tests. Questionnaire responses suggest that initial briefings were not always given in the early periods of the survey, but became more common as time went on.

Although not studied at Porton, there is no doubt that research into the common cold and influenza was conducted elsewhere and that it involved Service personnel. Various trials were conducted in the 1940s and 1950s of vaccines to counter influenza<sup>17</sup>, for which Service personnel were recruited. These trials were organised by the Medical Research Council under the aegis of the Ministry of Health. RAF personnel were recruited for trials of influenza vaccine in a few studies in the 1960s.

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<sup>15</sup> Annex H

<sup>16</sup> Chapter 21, Section 21.5

<sup>17</sup> Chapter 6, Section 6.2

The Common Cold Research Unit (CCRU), based at Harvard Hospital in Harnham Down about 8 miles from Porton, was set up under the direction of the Medical Research Council in 1946. The CCRU recruited volunteers to take part in cold and influenza research<sup>18</sup> by means of posters and notices in the open press. There is evidence that some notices calling for recruits for the CCRU appeared in Service administrative orders, and that Service personnel attended the CCRU (albeit off duty). No connection between the CCRU and Porton has been uncovered by the survey. The CCRU did have regular contact with the MRE, which itself developed injection devices for mass immunisation which were tested on Service volunteers (at Porton and elsewhere) especially recruited for that purpose<sup>19</sup>.

Many ex-Servicemen have contacted the Porton Down Helpline to report clear recollections of attending Porton, but for whom no records exist. Over the period covered by the survey Servicemen and Servicewomen attended the Defence Nuclear Biological and Chemical Defence Centre, based at Winterbourne Gunner about 3 miles from Porton to undergo routine chemical warfare training. Porton had close links with Winterbourne Gunner and it is possible that staff from Porton may have visited the establishment and spoken to the trainees about the PDV programme or even that some of the facilities at Porton were used by Winterbourne Gunner to undertake chemical warfare training. The Survey has not, however, found any written documentation to prove that this was the case.

## Information given before experiments

Information given to volunteers before individual studies<sup>20</sup> is cited in some technical reports. Commonly, these state that the volunteers were told about the nature of the study and their right to refuse to take part. In some cases, the name of the agent was given: "nerve gas" was referred to instead of, say, "GB" (Sarin). In studies with psychological incapacitants, the name and the nature of the substance used was sometimes intentionally not given so as not to influence the volunteer's behaviour while under study. The recollections of volunteers suggest some variability in the information imparted before studies in the early part of the period covered by the survey.

## Consent

The issue of consent proved difficult to interpret<sup>21</sup>. Volunteers' recollections generally suggest that they were not asked if they were content to participate in studies, at least during the 1940s to 1960s. It is possible that staff at Porton took the view that if the right to withdraw from a study or to refuse to start a study had been explained (in the notice or verbally at Porton), volunteers who chose to carry on were giving their consent implicitly to this taking place. Certainly, volunteers who wanted to refuse were allowed to do so: instances throughout the period of the survey have been found<sup>22</sup>, but what this says about the nature of consent is difficult to assess.

Signed consent was introduced by Porton in 1987<sup>23</sup>, under which a volunteer signed to say that the study had been explained to him/her in terms they could understand and that they agreed to participate<sup>24</sup>. This procedure had originally been suggested by the Admiralty in 1959. The Admiralty wanted volunteers to sign a document as tangible evidence that they understood the nature of the study and what it might involve by way of danger and discomfort, and that they were willing to undergo it. In subsequent discussions between the Services, this was seen as some form of "blood-chit" absolving the Services from any liability

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<sup>18</sup> Chapter 6, Section 6.1

<sup>19</sup> Chapter 6, Section 6.3

<sup>20</sup> Chapter 21, Section 21.6

<sup>21</sup> Chapter 21, Section 21.7

<sup>22</sup> Annex J and study narratives

<sup>23</sup> Chapter 21, Section 21.7

<sup>24</sup> Annex K

in case of injury. The introduction of such blood-chits was condemned by each of the Services and the idea was therefore discarded.

## Chemical warfare work at Porton

From its inception Porton has conducted defensive CW research and has been responsible for developing equipment and medical treatments to protect the UK Armed Forces from chemical warfare attacks. Sometimes, Porton has searched for chemical warfare agents for the UK to use in retaliation for enemy chemical warfare attacks<sup>25</sup> or for agents suitable for use in civilian settings to help authorities to control riots<sup>26</sup>. The broad thrusts of defensive and offensive work have followed UK Government policy on chemical warfare<sup>27</sup>. During the period covered by the survey the detail of Porton's work, within the framework of Government policy, has been directed by its superior government department (in succession, the Ministry of Supply, the War Office and finally the MOD) and through various high-level committees.

In the immediate post-war years, the Chemical Defence Advisory Board and various subordinate committees were established to advise Porton on different aspects of chemical warfare work. About half the CDAB members were drawn from academia and industry, and this level of representation of "outsiders" was mirrored in the other committees. The CDAB and the committees were not established to monitor the conduct of human studies at Porton *per se*, but sometimes the academic members advised on safety<sup>28</sup>.

Neither were these bodies charged with authorising the human studies conducted by Porton. Before the 1950s Porton from time to time sought approval for types of human studies from the Army<sup>29</sup>. The 1950s saw Ministers involved in the approval of some studies, and this was devolved to one of the CDAB committees in the early 1960s. It was not, however, until the formation of the Applied Biology Committee (ABC) that a body was set up specifically to advise on safety and ethics. The ABC, like the earlier CDAB committees, had members drawn from universities and university hospitals.

In 1964, an internal committee at Porton was established, - the Committee for the Safety of Human Experiments (COSHE) - which scrutinised proposals for human studies to ensure they were safe. In 1965, the Applied Biology Committee (ABC), a body with government and external members, was set up to advise the COSHE on the ethics of human studies. In the early 1970s the role of the ABC was taken on by the Medical Committee (MC), which also had non-government members. The MC established an Independent Ethics Sub-Committee in 1987.

## Human Studies at Porton Down

Virtually all the chemical warfare human studies conducted by Porton<sup>30</sup> over the period covered by the survey fall into one of the categories shown at Fig 1. Some of the studies did not involve volunteers being exposed to chemical warfare agents. It is important to realise that Porton's work was undertaken in response to military requirements<sup>31</sup>. Hence, for example, defensive equipment and medical treatments had to protect the Armed Forces while still enabling them to fight efficiently. The survey describes in detail the human studies of the type shown in bold at Figure 1.

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<sup>25</sup> Chapter 2, Section 2.1 - 2.2

<sup>26</sup> Chapter 1, Section 1.2

<sup>27</sup> Chapter 4, Section 4.1

<sup>28</sup> Chapter 4, Section 4.2 and Figure 4.1

<sup>29</sup> Chapter 4, Section 4.3

<sup>30</sup> Chapter 2, Section 2.3

<sup>31</sup> Chapter 2, Section 2.1

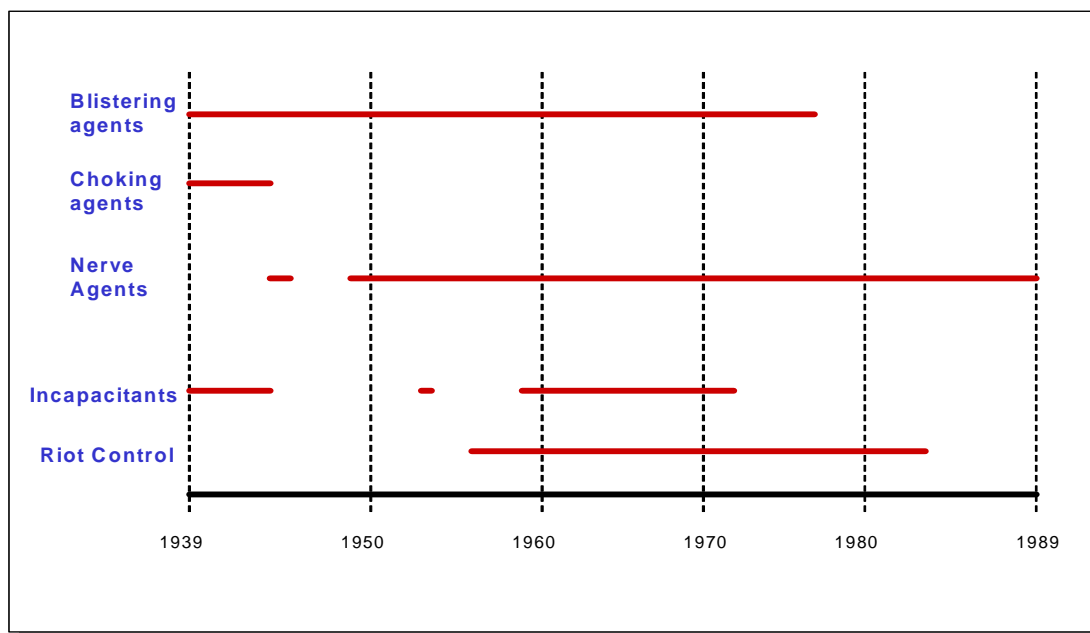
**Figure 1 - Porton Down Volunteer Programme Chemical Warfare Trials**

<b>Theme</b>	<b>Subject</b>	<b>Nature of study</b>
Effectiveness of agents	<b>Determination of minimum effective dose</b>	Typically, the symptoms and effects were studied. Some of these studies were comparative: does agent A produce effects at doses lower than agent B?
	<b>Determination of incapacitating dose</b>	Studies to identify the dose which hampered military performance. Many studies saw volunteers attempting tasks before and after being dosed with an agent.
	<b>Relationship between dose and symptoms</b>	Studies sought to find out if there was a clear relationship between doses and the symptoms induced. Results might be used to estimate lethal dose levels.
	<b>Detection of agent</b>	Volunteers were exposed to low doses to find out if they could detect the agent by their senses (typically, by smell) or by symptoms.
Protection	<b>Normal service dress</b>	Volunteers tested the protection afforded by normal service clothing. Sometimes, normal clothing was dusted with protective powders or impregnated with charcoal.
	<b>Protective clothing</b>	Studies to assess if fabrics being considered for protective clothing protected the wearer from liquid agents. Usually, pieces of fabric were attached to a volunteer's arm and drops of liquid agent placed on the fabric.
	Patch tests of rubbers for respirators	Chemical warfare agents were not used in these studies. Patches of rubber mixes would be fixed to a part of the body to find out if they caused irritation.
	Respirators	Studies to find out if respirators, properly fitted, were effective in protecting the wearer from chemical warfare agents. Some studies involved a chemical warfare agent, others an innocuous substance.
	Effect of wearing protective clothing	Chemical warfare agents were not used in these studies. Studies might determine the effect on physiology and performance of wearing protective clothing.
Treatments	<b>Skin decontamination</b>	Typically a drop of liquid chemical warfare agent would be placed on the skin and different ways of decontamination would be assessed.
	<b>Eye effects</b>	Different types of eye-drops were assessed in alleviating the symptoms after the eye had been exposed to either chemical agent vapour or liquid.
	<b>Poisoning</b>	Studies of the effectiveness of treatments in alleviating or preventing the symptoms induced by chemical warfare agent poisoning.
	<b>Physiological effects of treatments</b>	Chemical warfare agents were not used in these studies, which sought to assess the effect on physiology and performance of the treatments themselves.
	<b>Ease of use of treatments</b>	Chemical warfare agents were not used in these studies. Some studies considered how easy it was for Servicemen to administer therapies by injection or take tablets.

Some human studies at Porton were unrelated to chemical warfare. Over the period covered by the survey Porton conducted studies into the effect of smog, for example, and military and occupational hazards<sup>32</sup>. Other studies involving volunteers sought to develop relatively innocuous simulants which could be used instead of chemical warfare agents in research work<sup>33</sup>.

Human studies relating to chemical warfare conducted over the period of the survey can be separated according to the agents they considered<sup>34</sup>. This separation is shown in Figure 2 below.

**Figure 2 - Chemical Warfare Agents - period of testing**



## Nerve agent studies

Nerve agents attack the body's nervous system, interrupting, among other things, muscular function. They are effective through various routes into the body: inhalation of vapour, liquid applied to the skin, and the absorption of vapour through the skin. The programme of nerve agent studies is summarised at Figure 3. So-called G agents, developed by Germany during World War II, were discovered in 1945 as the Allies swept across Europe. G agents represented a considerably greater threat than the "traditional war gases", such as mustard, and were referred to by the Germans as the "Ideal War Gas". Concerns over the capture of nerve agents from Germany by Russia, and the policy decision to develop nerve gas weapons for the RAF and the Army prompted a large programme of studies.

Human studies with nerve agents were conducted initially with G agents (GA, GB, GD, GE and GF)<sup>35</sup>. Studies were of three types: vapour inhalation; the effect of vapour on the eyes; penetration of the skin and clothing by liquid. Each of these types of studies was done with G agents from 1945 to 1953. The studies mainly sought to understand the effects of G agents on man, and to estimate threshold and harassing dose levels and to provide results from which lethal doses could be extrapolated. Human studies with G agents were suspended in

<sup>32</sup> Annex A

<sup>33</sup> Annex B

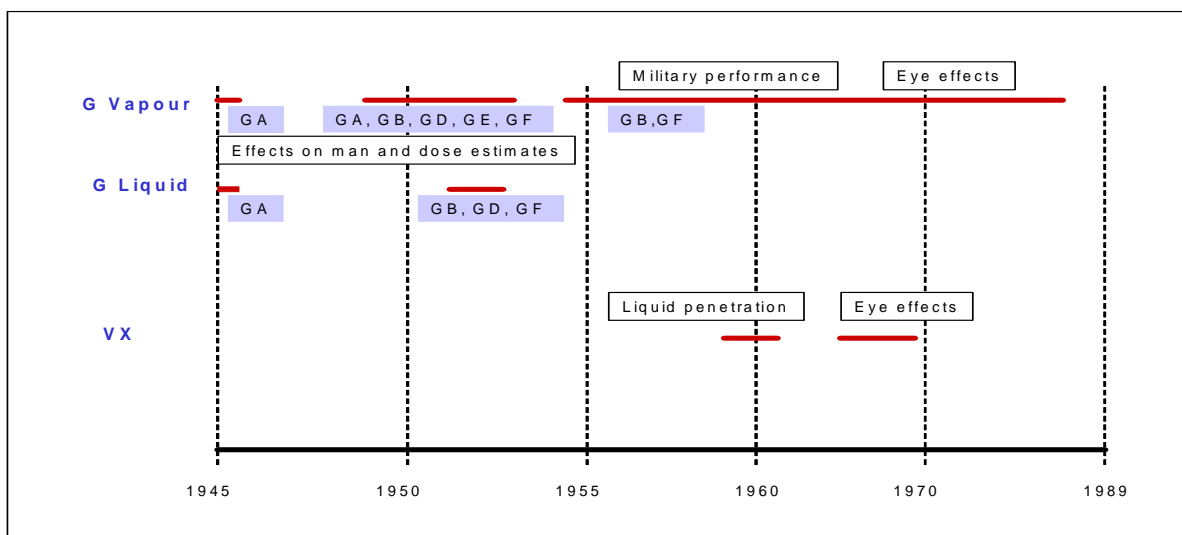
<sup>34</sup> Chapter 3

<sup>35</sup> Chapter 8 and 9

1953, after a Service volunteer died following a study in which drops of liquid GB were placed on material attached to his arm.

After an enquiry, and with Ministerial approval, G agent studies re-commenced in 1954, but under certain conditions<sup>36</sup>. Only GB (otherwise known as Sarin) was to be used, and at lower exposure levels than previously (although exceptionally a couple of studies were done with GF). GB studies after 1954 were confined to vapour work. Most of the GB studies after 1954 sought to understand the effect on military performance. A series of studies considered whether exposure to G agents might cause permanent damage, and the medical histories of volunteers who had been exposed to GB were investigated in a series of follow-up studies<sup>37</sup>.

**Figure 3 - Nerve Agent Studies**



From 1954, less effort was devoted at Porton to G agent work for a number of reasons, including:

- work was dominated by human studies of treatments for nerve agent poisoning.
- the decision to abandon the development of nerve agent weapons for the RAF and the Army<sup>38</sup>.
- the discovery in 1953 of a new class of nerve agents: the V series<sup>39</sup>. V agents are much more toxic than G agents, and were sometimes referred to as the "New terror". From 1958-1969 studies were conducted with one of the V agents, called VX. At the time they started, permission to conduct human studies with nerve agents had to be given by Ministers. This was a consequence of the conditions imposed on nerve agent studies following the suspension in 1953. However it is not quite clear when permission for VX studies involving Service volunteers was obtained<sup>40</sup>. Studies with VX involving Service volunteers considered the skin penetration of liquid VX and the effect of VX vapour on the eyes. Studies of the inhalation of VX vapour were conducted only with volunteers from the Porton medical staff.
- the interest in incapacitating agents.

<sup>36</sup> Chapter 9, Section 9.1

<sup>37</sup> Chapter 9, Section 9.6

<sup>38</sup> Chapter 4, Section 4.1

<sup>39</sup> Chapter 10

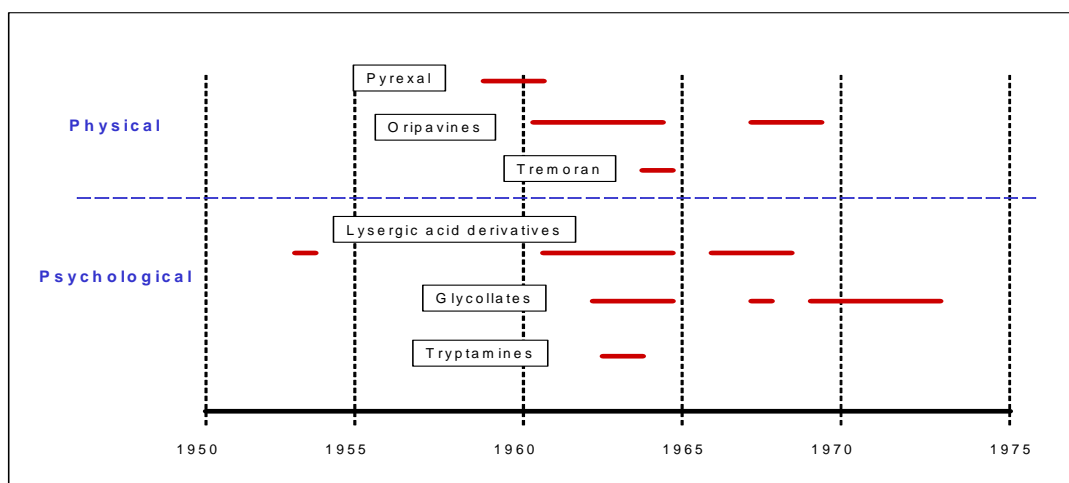
<sup>40</sup> Chapter 10, Section 10.1

## Incapacitating agent studies

Incapacitants, as the name suggests, seek to render the enemy incapable of effective military action by affecting the mental processes and perception (examples include Lysergic Acid derivatives (LSD); LAE; glycollates and tryptamines) or by upsetting some aspect of physiology e.g. body temperature (examples include pyrexal; oripavines; tremoran; various tear gases and sternutators).

The interest in incapacitating agents arose during a review of chemical warfare in the late 1950s and early 1960s, prompted partly by the concern that they might prove to be a threat to the UK Armed Forces and partly by an interest in developing them as offensive agents for the UK Services<sup>41</sup>. The main programme of human studies started in 1959, and is summarised at Figure 4. There was a short study with LSD in 1953 and 1954<sup>42</sup>, but this was specially commissioned to investigate whether or not LSD had any value as a "truth drug". In the main programme a distinction was drawn between psychological incapacitating agents<sup>43</sup> and physical incapacitating agents<sup>44</sup>.

**Figure 4 - Porton Down Volunteer Programme - Incapacitant agent trials.**



A battery of medical screening tests was developed for human studies of psychological incapacitating agents to ensure that volunteers were mentally suitable<sup>45</sup>. Trials included LSD, LAE, another lysergic acid derivative BZ, tryptamines and a substance referred to as T3436.

Some substances which incapacitated physically were rejected by Porton as unsafe for human studies; notably drugs whose primary purpose was to attack blood pressure levels and to induce vomiting. The dominant programme of work with physical incapacitating agents featured oripavine derivatives which have a similar effect to morphine. Pyrexal, which increases body temperature and tremoran, which can induce muscle tremors and muscular weakness<sup>46</sup> were investigated in short human studies. Uncertainties remain over some of the agents used in this programme of work, notably nutmeg, captagon<sup>47</sup> and aldactone<sup>48</sup>.

<sup>41</sup> Chapter 4, Section 4.1

<sup>42</sup> Chapter 11, Section 11.2

<sup>43</sup> Chapter 11

<sup>44</sup> Chapter 12

<sup>45</sup> Chapter 11, Section 11.1

<sup>46</sup> Chapter 12, Section 12.1 - 12.4

<sup>47</sup> Chapter 11, Section 11.5 - 11.6

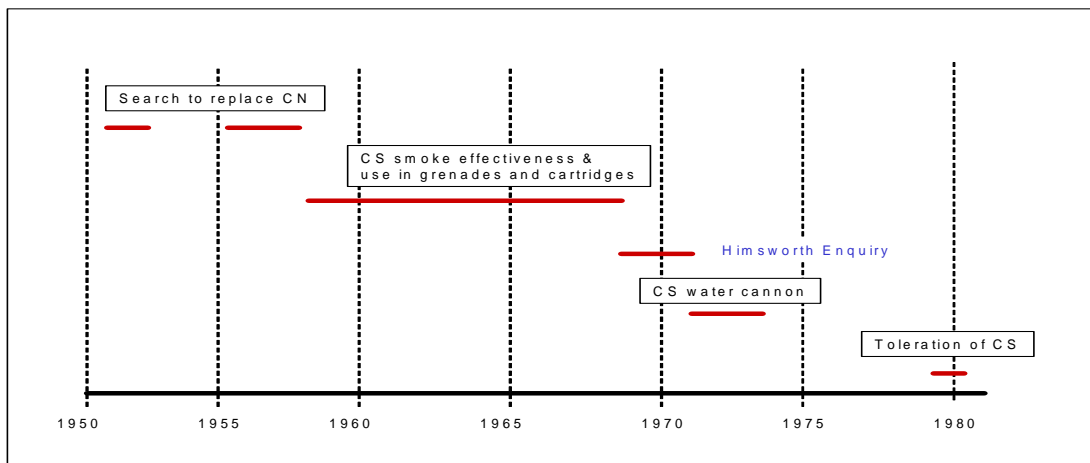
<sup>48</sup> Chapter 12, Section 12.5

Human studies with some of the incapacitating agents were suspended by Porton in 1965. Porton medical staff were concerned about the ethics of involving volunteers in studies<sup>49</sup> and as a result of their discussion with medical experts formed the Applied Biology Committee to act as a guide to Porton on ethical conduct. With reassurance from medical experts and the ABC, the programme of work with incapacitants re-commenced later that year.

## Riot control agents

Riot control agents are strictly physical incapacitating agents, but they are considered separately because they were developed for use in civilian situations. By 1939 CN, a tear gas, was in use as a riot control agent. During World War II Porton trialled many different tear gases and sternutators (agents which induce sneezing fits) to determine their use in war. Studies related to riot control in the period covered by the survey began in the early 1950s, and a short series of studies with alternatives to CN was conducted in 1951-1953. A larger series of tests took place between 1956-1958, from which CS emerged as the replacement for CN. A summary of CS studies is given at Figure 5. Briefly, from 1957-1969 studies explored the effectiveness of CS as a smoke dispersed from grenades and cartridges<sup>50</sup>, with CS first being used in the UK in August 1969. As a consequence of public and press concerns about the effects of CS on members of the general public the Home Office set up an enquiry, conducted by the Himsworth Committee to look into the medical and toxicological effects of CS<sup>51</sup>. The enquiry ran until late 1971. Some trials were conducted at Porton to support it.

**Figure 5 - CS Studies**



From 1971 trials with CS were largely conducted as part of the development of the CS water cannon<sup>52</sup>. Various CS solutions were tested for their irritancy on small areas of skin.

CR was developed as a replacement for CS in the early 1960s. The first series of studies investigated the toxicity of CR and compared its effectiveness with that of CS. CR was found to be much less toxic than CS<sup>53</sup> but more striking in its effects on humans. CR is more soluble in water than CS, so many human studies considered devices to project CR solutions<sup>54</sup>. For example, during the period:

<sup>49</sup> Chapter 13

<sup>50</sup> Chapter 14, Section 14.1 - 14.2

<sup>51</sup> Chapter 14, Section 14.3

<sup>52</sup> Chapter 14, Section 14.4

<sup>53</sup> Chapter 15, Section 15.2.2

<sup>54</sup> Chapter 15, Section 15.3 - 15.5

- 1968-1975 volunteers trialled CR in a self-protection aid device, which looked like a conventional spray can, and was intended for use against the face of an attacker.
- 1971-1973 volunteers took part in water cannon trials.
- 1973-1974 volunteers trialled CR in squirt devices. These devices projected smaller volumes of CR solution than a water cannon and were based on conventional fire extinguishers.
- 1974 onwards saw various miscellaneous CR studies, including some work undertaken jointly with the Medical Research Council<sup>55</sup>. Although CR is less toxic and more effective than CS, it is more persistent. So, if it were used in civilian settings some form of active decontamination procedure would be required. CS, in contrast, is highly volatile: it evaporates from solid form. Surfaces contaminated with CS would not require active decontamination. A series of studies was therefore undertaken to assess methods of CR decontamination<sup>56</sup>.

In addition to these CS and CR studies, some miscellaneous work was undertaken relating to riot control<sup>57</sup>. Screening techniques to compare irritant agents were investigated. For a short time the technique of instilling a small drop of liquid irritant into the conjunctival sac of the eye was considered. However, this was abandoned in favour of the "blister base technique", in which a blister was raised and excised followed by the application of a drop of an irritant to the base of a blister.

As part of the searches from which CS and CR emerged, studies considered the value of Bitrex and re-assessed the skin effects induced by CN<sup>58</sup>. One substance, referred to most efficiently as T4423, started life as a candidate riot control agent, but for various reasons was ultimately considered as a training simulant<sup>59</sup>.

## Other human studies with chemical warfare agents

Studies with nerve agents, incapacitants and riot control agents form the main blocks of studies undertaken with chemical warfare agents after World War II.

The predominant concerns during World War II were to develop new agents and new munitions with which they, and the already-available war gases could be delivered. Human studies and field trials considered the two main categories of war gases; vesicants (Mustard Gas (H) and Lewisite (L), for example) and irritant compounds (Bromobenzyl cyanide (BBC), Chloroacetophenone (CN), Adamsite (DM)) which would cause burns or blisters when contact through liquid or vapour was made with the skin.

Vesicant studies<sup>60</sup> tested substances typically by placing a drop of their liquid on the arm of a volunteer and comparing the effects with those of a drop of either L or H. Hundreds of substances were tested in this way, and most of them were rejected as being less effective than H or L. The nitrogen mustards (HN-1, HN-2 and HN-3) were discovered through such tests. Other studies, of the same type, tested variants of H and L (including gelled or "sticky" H and L), and mixtures of them. The effects of H, L and nitrogen mustard vapour against the skin and eyes were evaluated in chamber tests. The relative sensitivity to H of skin at different body sites was explored.

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<sup>55</sup> Chapter 15, Section 15.6

<sup>56</sup> Chapter 15, Section 15.7

<sup>57</sup> Chapter 16

<sup>58</sup> Chapter 16, Section 16.2 -16.3

<sup>59</sup> Chapter 16, Section 16.4

<sup>60</sup> Chapter 17, Section 17.2

In a similar way, alternatives to existing irritant compounds were explored, typically by exposing volunteers to low concentrations in the chamber and comparing the effects with those known to be produced by BBC and CN. Many hundreds of compounds were tested in this way<sup>61</sup>. Those that were deemed promising were investigated further, and tests were developed and tried which could measure the effect they had on performance<sup>62</sup>. This work suggested the degree of contamination which would need to be delivered by munitions in order to harass the enemy. Studies explored "harassment curves" for BBC and CN, to link the degree of contamination with the percentage of men likely to be harassed<sup>63</sup>. Allied to this work were studies to explore how men developed tolerance to irritant compounds, and whether tolerance, once developed, was effective for long periods and against many irritants.

Several field trials were conducted with vesicants and irritant compounds<sup>64</sup> to test new methods of delivery and new forms of agent (such as gelled mustard), and to assess the effect of ammunition. Field trials of this type with H often produced burns of "casualty severity" among the volunteers who took part, many of whom were subsequently unfit for duty for up to a month afterwards.

Typical of the field trials considering ammunition were those which tested the German 7.92 mm armour-piercing bullet which contained a small amount of CN in the base. Studies involved these bullets being fired at vehicles, and then measurements being taken of the degree of contamination that resulted inside. Sometimes, volunteers were positioned in the vehicle, notably in a series of tests with glass grenades filled with CN thrown against a tank.

Similar trials were done with other small rounds of ammunition. A volunteer died in 1944 after one trial, in which a 25 mm round containing an irritant compound was fired at a tank. The volunteer was inside the tank, with others and a member of the Porton staff. Unexpectedly, a metal shard was loosened by the impact of the round and struck the volunteer in the neck. Field trials were done after World War II to explore munitions charged with nerve gas. Very often these involved firing munitions at a tank or armoured fighting vehicle to find out the level of contamination that resulted inside the vehicle. None of these trials with nerve gas employed volunteers: they used chemical samplers or small animals in cages deployed inside the tank.

Work with chemical agents after World War II other than those already covered was quite sparse. Investigations were mounted into the sensitivity of the skin to H, which involved repeated application of drops to the same site or in different concentrations. Work with H at Porton was stopped in the late 1970s because of concerns over carcinogenicity<sup>65</sup>. The other work mentioned here is the development of dye-markers<sup>66</sup>. Dyes were developed for use in riot control devices, so that rioters who ran away from the scene could be identified later. However, the dyes developed at Porton had other applications: as additives to simulants and training agents to help in the analysis of field trials and training exercises.

## Treatments

Human studies to develop treatments were conducted throughout the period covered by the survey. The largest programme of work (which still continues today) sought to develop treatments for systemic nerve agent poisoning. Two forms of treatment were explored in human studies; prophylactics, which guard against the effects of poisoning, and therapies, which treat the effects. Prophylactics were developed as tablets, and in practice are usually taken on a regular basis whenever the threat of nerve agents being used against the Armed

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<sup>61</sup> Chapter 17, Section 17.3.1

<sup>62</sup> Chapter 17, Section 17.3.2

<sup>63</sup> Chapter 17, Section 17.3.3

<sup>64</sup> Chapter 17, Section 17.3.4

<sup>65</sup> Chapter 18, Section 18.2 - 18.3

<sup>66</sup> Chapter 18, Section 18.4

Forces is felt to exist. For example, Service personnel serving in the Gulf War started taking prophylactic tablets before they arrived in theatre and continued to take them while they were there. Therapies, taken after exposure to nerve agents, were developed as either injections or tablets.

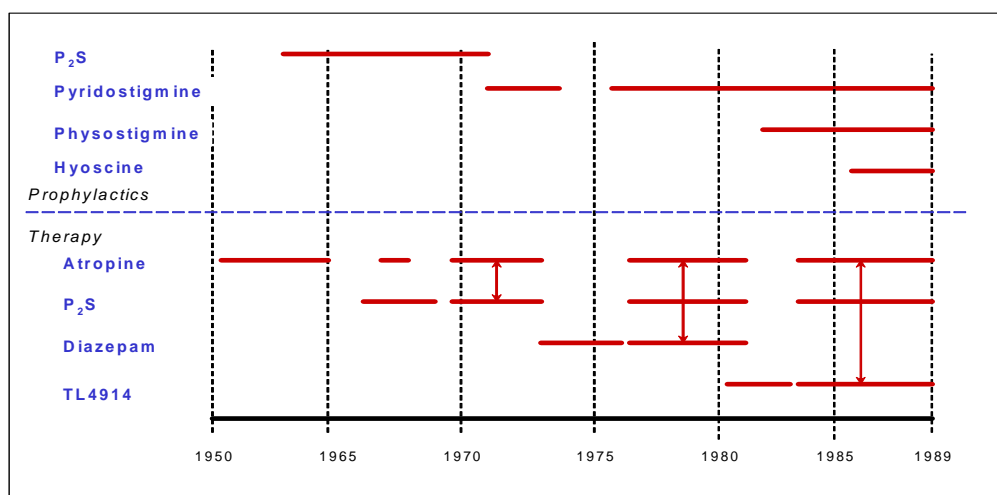
The forms of treatment developed for nerve agent poisoning in human studies at Porton fall into distinct categories<sup>67</sup>.

- Therapies which treat the effects induced by nerve agents. Atropine sulphate falls into this category. Diazepam (whose trade name is Valium), and a soluble form of diazepam referred to as TL4914, also sit here as they alleviate the tremors and convulsions induced by severe nerve agent poisoning.
- Therapies which reverse the action of nerve agents. P<sub>2</sub>S for example, eases the neuromuscular (NM) block induced by nerve agents.
- Prophylactics which protect the body from the action of nerve agents. Examples here are pyridostigmine bromide, physostigmine salicylate and hyoscine.

The majority of human studies with these treatments did not involve volunteers being exposed to GB. Instead, the effect of each treatment on physiology and performance was explored; various methods were used to assess performance, including car driving and memory tests<sup>68</sup>. Studies explored effective dose levels and ways to administer treatments; the size and shape of tablets, and the design of injectors for therapies.

Therapies were studied in combination, as well as individually. Initially, P<sub>2</sub>S and atropine were considered together. Diazepam was added, but eventually replaced with TL4914<sup>69</sup>. Figure 6 shows the human studies with nerve agent treatments. The therapies studied in combination are connected by red arrows. Prophylactics were also studied in combination with therapies. The effects of many of these treatments were studied with volunteers who continued to work at their own units, and some work with atropine was conducted with volunteers at UK military units in Iraq and the Far East.

**Figure 6 - Human Studies with nerve agent treatments**



<sup>67</sup> Chapter 19, Section 19.1 - 19.6

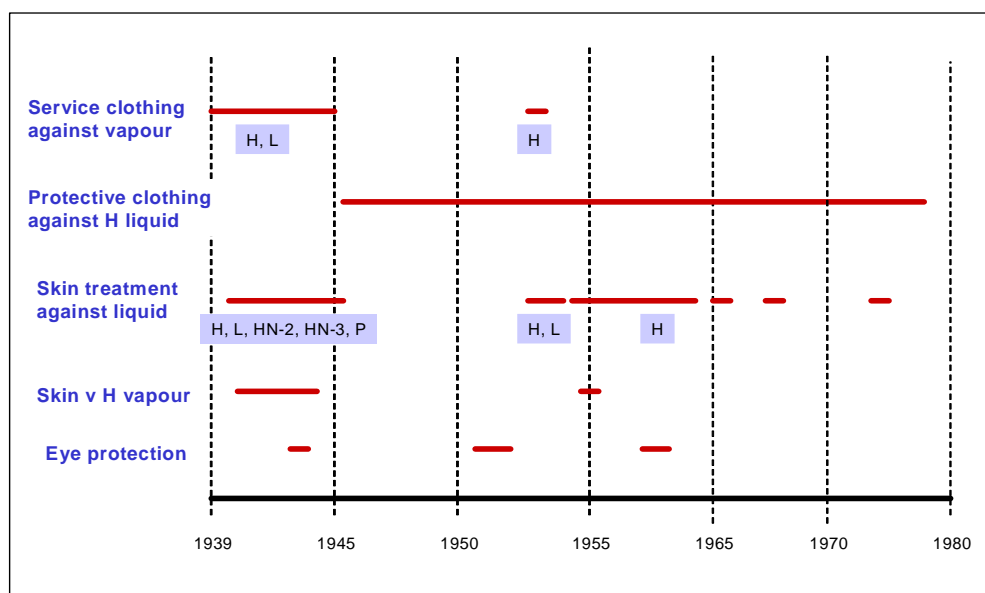
<sup>68</sup> Chapter 19, Section 19.7

<sup>69</sup> Chapter 19, Section 19.5

Treatment work during World War II was devoted to protecting the skin against the "traditional" war gases. Various forms of treatment were considered: impregnating normal Service clothing with powder or charcoal to protect the skin from H and L vapour; ointments and creams to decontaminate the skin from liquid H, L and nitrogen mustards (HN-1, HN-2, HN-3) and to protect the skin from vapour effects; and methods of treating H blisters. Methods of decontaminating clothing, equipment and food were assessed. Studies explored whether protective clothing prevented the passage of vesicants in liquid form (sometimes referred to as "penetration studies")<sup>70</sup>.

Some of these studies continued after World War II. In particular, many penetration studies were done to test a wide range of fabrics, although post-war work considered only H liquid. World War II work on skin decontamination and treatment was extended in attempts to find one procedure which was effective against all forms of liquid agent, notably H, G and V. Human studies were confined to H: G and V work being done with animals or in the laboratory. Various eye treatments were considered<sup>71</sup>. Figure 7 gives an overview of human studies investigating treatments. Some other treatments, taken internally were considered: cortisone acetate, moryl, probanthine, tolazoline and ephedrine hydrochloride<sup>72</sup>. Reports of studies with these treatments have not been found, so it is not possible to say why they were investigated.

**Figure 7 - Overview of human studies investigating treatments**



<sup>70</sup> Chapter 20, Section 20.1.2 - 20.2.5

<sup>71</sup> Chapter 20, Section 20.4

<sup>72</sup> Chapter 20, Section 20.3

## Ethics

From an ethical perspective the survey has considered eight themes:

- The relationship between the volunteer and the researcher, particularly any dependency that might exist.
- How consent was obtained and the requirement for some tangible evidence that it had been obtained.
- Whether a concept of "risk" for volunteers existed, and the nature of the risk.
- The extent of information given to the volunteer about the study, and the form in which it was given.
- Compensation.
- Payments and inducements.
- Ethics committees.
- The need for prior research before using humans.

Porton's practice in these areas is discussed fully in the main Historical Survey and touched upon elsewhere in the summary.

### Ethics codes and guidelines and practice

Over the period of the survey various national and international bodies published codes and guidelines concerning the ethics of medical research with volunteers. The contents of these codes and guidelines, and an analysis of how they were implemented in practice over the period covered by the survey has been produced by a qualified academic, Dr Alasdair Maclean of the University of Dundee. The codes and guidelines were recommendations; they did not compel researchers to follow them. What the codes and guidelines said about the eight themes considered by the survey has been extracted and included in the main text<sup>73</sup>.

The way in which these codes and guidelines were implemented in practice in UK medical circles over the period covered by the survey has been analysed, independently of the MOD<sup>74</sup>. The analysis is not intended to be a definitive statement of the practice of research with healthy human beings. Indeed, it is difficult now to ascertain in detail how the ethical themes were implemented in, say, the 1940s and 1950s. Notwithstanding that caveat, the following general points might be made<sup>75</sup>:

- The Nuremburg code was felt by most researchers to be inapplicable to them, and it had little if any impact in practice. In the second half of the 1950s, public, media and political scrutiny of research activity increased and culminated in recommendations from the Medical Research Council and the Declaration of Helsinki in 1964. However, these publications were simply guides and concentrated mostly on research conducted with patients, as opposed to healthy volunteers.

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<sup>73</sup> Chapter 22, Section 22.2

<sup>74</sup> Chapter 22, Section 22.4

<sup>75</sup> Chapter 22, Section 22.6

- In the latter part of the 1960s, publications by prominent medical men (Papworth in the UK in 1967 and Beecher in the US in 1966) coincided with the emergence of bioethics as an academic discipline. Medical research with healthy human beings drew more attention in the 1970s (and increasingly so in the 1980s), and guidelines and codes became more detailed.
- Ethics committees were suggested as a medium for ethical supervision of research, and in the 1970s and 1980s important advances were made with ethics committees. Nonetheless, those that were introduced were inconsistent in both membership and practise.
- "Informed consent" was not a term that had a common definition during the period covered by the survey. In the early period, it was largely accepted that for research involving volunteers consent was required. However, the definition of consent varied: most commonly, it was viewed simply as an agreement by the volunteer to participate in the research. The amount of information disclosed to a volunteer was seen as that necessary merely to gain the volunteer's co-operation. Information disclosure was not seen as a priority until the mid-1970s. Even then it was subjected to both criticism and resistance, as researchers argued that it was futile since the subjects were unable to understand the information.
- By the end of the 1980s, the regulations of human research, although far improved from those in place in 1939, still had a long way to go. But the 1970s and 1980s (particularly, of the decades covered by the survey) saw more attention being given to the ethics of medical research with healthy volunteers and mark a departure from the approach, prevalent in the past, of leaving ethics to the conscience of the individual researcher.
- The ethics of medical research drew more attention in the 1970s (and increasingly so in the 1980s), and guidelines and codes became more detailed and seem to have been implemented more quickly.
- Nonetheless, there was still a time-gap between the publication and subsequent widespread implementation.

Sir Ian Kennedy's assessment of Porton's conduct appears at the end of the survey<sup>76</sup>. It draws on the descriptions of the trials conducted by Porton, the information presented on how service volunteers were recruited, and on Dr Maclean's analysis of ethics codes/guidelines and practice. No attempt has been made by the MOD to summarise Sir Ian's assessment, to avoid any inadvertent changes in meaning on language.

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<sup>76</sup> Chapter 23

## **Acknowledgements**

The MOD would like to thank various people for their assistance and advice during the survey. First and foremost, the MOD would like to express its deep appreciation to Sir Ian for giving so much valuable guidance to, and for his considerable patience with, the survey team. It has been a pleasure having Sir Ian act in the role of independent supervisor.

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- The Imperial War Museum
- The Public Records Office
- The (erstwhile) Director of the Medical Research Council's Common Cold Research Unit

