Reconstructing Exposures from the UK Chemical Warfare Agent Human Research Programme

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Received 8 January 2007; in final form 23 February 2007; published online 30 June 2007

The UK government has carried out a research programme studying military capability under conditions of chemical warfare at a facility at Porton Down, Wiltshire, since World War I. In 2001 the Ministry of Defence commissioned a cohort study to investigate the long-term health effects on military veterans of their participation in this programme. We assessed the availability and quality of exposure assessment data held in the archive at Porton Down for the purpose of this study. This involved looking in detail at exposure data in a sample of 150 veterans and undertaking a general review of all available records held in the archive. These sources suggested that the Porton Down records were largely complete and included sufficient identifying information for linkage with service personnel data and with national mortality and cancer registration records. Servicemen usually had multiple tests so data were most readily available in a test-wise format, allowing subsequent aggregation of tests by individual. The name of the chemical used in each test could be determined for most tests and most of the named chemicals could be categorized into major groups for epidemiological analyses. For the major groups (vesicants and nerve agents), quantitative data were available on exposure and on acute toxicity. Standardization will be required of the several different units which were used. Based on this study, exposure assessment for the cohort study of Porton Down veterans will involve abstraction of the name of the chemical used in each test, with quantitative data on exposure and acute toxicity for vesicants and nerve agents. Our results here show that experimental records at Porton Down offer a unique and valuable resource for reconstructing the chemical exposures used in this research programme. The resulting cohort study has the potential to provide information which will assist in understanding the long-term health impact of chemical warfare agent exposure on these veterans.

Keywords: chemical warfare agents; exposure; mustard gas; sarin

INTRODUCTION

Chemical warfare agents, first used in World War I (WWI), are designed to have lethal, incapacitating or unpleasant physical effects in humans and much is known about their acute toxicity (Evison et al., 2002). Less is known about their long-term health effects. The small number of epidemiological studies with long-term follow-up have shown some evidence for an increased risk of respiratory cancers in the US and UK servicemen exposed to sulphur mustard during combat in WWI (Case and Lea, 1955; Beebe, 1960; Norman, 1975) and also among workers engaged in sulphur mustard gas manufacture (Wada et al., 1968; Easton et al., 1988) but not in people exposed to sulphur mustard in human experiments (Bullman and Kang, 2000). In addition, reports of clinical follow-up in people exposed to sulphur mustard during the Iran–Iraq war have been published (Balali-Mood et al., 2005). While persisting symptoms have been reported in civilians exposed to sarin in the Tokyo terrorist incident (Nishiwaki et al., 2001; Miyaki et al., 2005), no excess of cause-specific mortality was seen in them or in people exposed to...
sarin in human experiments (National Research Council, 1982; Page, 2003). Detailed exposure information is typically lacking after the use of chemical warfare agents in warfare or by terrorists and is variably available for occupational studies, meaning that only limited exposure–response analyses can be carried out. However, with human experiments, considerable exposure information may be available. Very few developed countries have had research programmes involving collection of detailed exposure information as part of human experiments (Pechura and Rall, 1993; Evans, 2000).

A British governmental research facility has been located at Porton Down since WWI. Along with laboratory-based research and animal toxicology, the facility runs a programme, mainly involving members of the armed services, of human research relating to military capability under conditions of chemical warfare (Carter, 2000; Evans, 2000; Ministry of Defence, 2006). It is not known how many servicemen were recruited to this programme since WWI, but in the 50-year period following the outbreak of WWII (1939–1989) up to 20 000 individuals are thought to have taken part (Ministry of Defence, 2006). The programme is known as the ‘human volunteer programme’ or the ‘service volunteer programme’ and groups of servicemen (and some servicewomen), known as ‘observers’, were recruited for visits that, in general, were expected to last up to 2 weeks. In practice, however, many veterans stayed for less than a week and very few veterans stayed for more than two (Bramwell, 1959; Ministry of Defence, 2006). Some people made repeat visits and may have been involved in many tests during each visit. Some tests involved exposure to chemical warfare agents or riot control agents; others involved trials of antidotes or of protective equipment without chemical exposure.

A US Institute of Medicine committee reviewed the comparable US human experiments involving mustard gas and lewisite (Pechura and Rall, 1993) and commented that ‘... morbidity and mortality studies should be accomplished ... comparing ... cohorts to appropriate control groups in order to resolve some of the remaining questions about the health risks associated with exposure to these agents’. Two cohorts have been followed in the US (National Research Council, 1982; Bullman and Kang, 2000; Page, 2003). In the UK, an important step has been taken with the start of a cohort study which includes 20 000 veterans who attended Porton Down between 1939 and 1989 together with 20 000 military controls, followed up for cause-specific mortality and cancer registration.

The study reported here was a precursor to the cohort study and, in it, we undertook a general review of the archive of historical documents made available to us at Porton Down and studied the records of 150 randomly sampled individual servicemen in detail to establish what information could be used in an exposure assessment for the cohort study. The questions we asked were the following: are records of the human trials available over the whole period 1939–1989? Are the records complete? Can individual servicemen be identified so that linkage is feasible with their military personnel records and, ultimately, national death and cancer incidence records? Did servicemen have one exposure at Porton Down or several; if several, to one chemical or several? Is the name of the chemical clearly documented so that servicemen with similar exposures can be amalgamated into exposure groups for analysis? Is the date of exposure recorded? Is there information on the intensity of exposure and on its duration, for use in quantitative exposure–response analyses? Is there information on acute toxicity (e.g. skin reddening or change in blood cholinesterase level) which can be used in dose–response analyses? Is there information on other important factors which may be potential exposure or effect modifiers, such as route of exposure or wearing of protective clothing?

METHODS

Availability of records

A collection of archival material dating back to 1920, mainly books of attendance records and experimental record books, was assembled at the Defence Science and Technology Laboratory at Porton Down in the 1970s, both as a historical collection and as an aid in responding to queries from veterans who had been participants in experiments. In July 1999, Wiltshire Police initiated enquiries into allegations of illegal human experiments at Porton Down (these enquiries were not subsequently taken forward to prosecution). These enquiries were known as ‘Operation Antler’ and covered the period 1939–1989 (Wiltshire Police, 2004). The archive was catalogued in 2000 by the police. The same archive was made available to us when this epidemiological research started in 2002.

The title of each item in the archive was noted, with the date of each first and last entry. Books containing lists of names and dates of attendance but no, or limited, experimental information were categorized as ‘administrative’ while those containing principally experimental information were categorized as ‘experimental’. All archival material that contained information on tests between 1939 and 1989 was included as a possible data source in this pilot phase. The archival material was briefly examined and key personnel were interviewed to obtain a general view of the completeness of the archive and of exposures during the human volunteer programme.

Comparison of subject numbers with contemporaneous annual reports

A database of participants in the human volunteer programme from 1939 to 89 compiled earlier by the
Ministry of Defence from these records was made available to us. We also searched the Porton Down library for annual reports relating to the human volunteer programme for the same period (Porton Down, 1963–1988) and consulted two Porton Notes and one Porton Medical Committee minute about the history of the human volunteer programme (Bramwell, 1959; Bradshaw, 1965; Kemp, 1974). Bradshaw’s (1965) document, ‘The service volunteer observer scheme’, was an addendum to Bramwell’s (1959) document, ‘History of the service volunteer observer scheme at CDEE’, and these two Porton Notes were treated as one. We compared the number of people in each calendar year from these four sources. We noted the years in which the Ministry of Defence database recorded >10 persons fewer than the smallest number noted in the contemporaneous annual and other reports relating to that year.

**Sample selection procedures**

A stratified random sample of 150 military service numbers was chosen from the database compiled by the Ministry of Defence. The database was stratified (in order to obtain 30 veterans per decade) according to the decade of the first visit to Porton Down, 1939–1949, 1950–1959, 1960–1969, 1970–1979 or 1980–1989. This sample of 150 service personnel ensured that adequate exposure information was provided for tests carried out in the later decades, when fewer veterans attended Porton Down. It was known that most veterans attended Porton Down in the early part of the study period. The military service numbers of 30 people were randomly selected from each decade. The selection by means of service numbers necessarily excluded any civilians, although small numbers of Porton Down civilian staff were known to have participated in the programme. The administrative and experimental books were then searched for all the information relating to each person’s first visit to Porton Down; any second or subsequent visits were not included.

**Extraction of the exposure data**

Each test during the first visit was reviewed. Tests were categorized as chemical or non-chemical. Where there was no exposure to chemicals (such as for personality tests, human performance tests and tests of new equipment under varying conditions), no data regarding the test were abstracted.

For chemical tests, the name of the chemical was noted and chemicals with one or more synonyms were recoded to the most common name. The title of the test, use of protective equipment, use of decontaminants, prophylactic agents or antidotes, the level and duration of exposure, and any quantitative acute toxicity data were recorded. The route of exposure was abstracted later. For the standardized mustard sensitivity tests and rubber patch tests (see below), only the occurrence of the test was documented because of the availability of exposure information from other sources.

Each chemical was classified into an extended categorization derived from that in the NATO Handbook on the Medical Aspects of NBC Defensive Operations (US Department of the Army, 1996) with assistance from Chemfinder (Chemfinder.com, 2004) and the Merck Index (O’Neill, 2001). This resulted in 16 categories which were: vesicants, nerve agents, riot control agents, incapacitants, lung-damaging agents, blood agents, choking agents, smokes, fuels and incendiary devices, herbicides, irritants, treatments, rubber mix tests, mustard sensitivity tests, other and unknown. Dermal patch tests of different rubber compounds were carried out in great numbers over the study period, we understand to assist in the specifications for protective equipment. Mustard sensitivity tests were routinely administered to exclude those with a known sensitivity to mustard from being re-exposed. Chemicals whose purpose was known but which did not fit the categories listed above were categorized as ‘other’ (e.g. dye, antiperspirant). Chemicals whose purpose was unclear were categorized as ‘unknown’ (e.g. those listed only by a code number).

**RESULTS**

**General review of the archive**

For the period 1939–1989 the Porton Down historical archive provided to us comprised 111 record books, categorized as administrative (n = 14) and experimental (n = 97) (Table 1). There were no gaps between the finish date of one administrative book and the start date of another, suggesting that this series of administrative books for this period was complete. It is known that experimental books covering part of 1963 and 1964 are missing (Ministry of Defence, 2006). It was clear that supplementary material (in the form of Porton Notes and other documents) may be available to assist indirectly by providing background information for the exposure assessment, but it was unclear in this study if any further direct information on the exposures of individuals was available.

Most administrative books were handwritten and all contained partial or complete information on some or all of the following: surname, forename, military service number, military rank, date of birth or age, military unit, and first and last dates of attendance. Some also recorded a number assigned to each volunteer on arrival, a laboratory number for blood tests, height and weight, and records of pay relating to the visit.

The experimental books were handwritten and contained extensive information whose content, style and quality varied widely between books, within
books, and over time (Fig. 1). Many results involving dermal exposures to vesicants were recorded in the form of pictograms (Fig. 1a), some results were recorded in table form (Fig. 1b), while others were in a diary format (Fig. 1c). Records made in the 1940s or 1950s were, in general, more legible than those made in later decades. Experiments in the books were usually, though not always, recorded chronologically. Individuals were identified in experimental books by surname only and other identifying information, such as forename or service number, was rarely documented. However, it was possible to link individual entries with those in the administrative books using the date of the test and the personal identifiers available.

Types of test

The types of test were varied. Most took place in a laboratory or environmental chamber on the Porton Down site. Others took place on the Porton Down ranges, an adjacent large area of chalk grassland. The range trials were intended to simulate conditions likely to be encountered on active service. Many tests were designed to test the protection afforded by, or decontamination of, normal uniform or protective equipment. Other tests were of the efficacy of decontamination procedures, prophylactic agents and antidotes.

Comparison with annual reports

The annual number of persons recorded in the Ministry of Defence database is compared with the numbers recorded in annual reports and Porton Down documents in Fig. 2. The Ministry of Defence database covered the period 1941–1989. The available Porton Down annual reports covered the periods 1946–1965 and 1965–1987, the Porton Notes the period 1946–1965 and the Medical Committee minute the period 1965–1987 (Bramwell, 1959; Bradshaw, 1965; Kemp, 1974). Where data from two or more sources were available, all points are plotted. The Ministry of Defence database shows that, over this period, the greatest numbers were recorded in WWII, with a second peak of visits in the 1950s. Broadly, the numbers from annual reports and other documents agree well with the numbers in the Ministry of Defence database, although in the years 1946, 1953, 1955, 1956, 1958, 1960, 1961, 1962, 1963, 1968, 1969, 1973, 1974, 1975 and 1981 the number from the database is 10 persons less than the number from other sources, possibly raising questions about the completeness of the historical archive.

Experimental data for sample of subjects

It proved very time consuming to abstract data relating to 150 specific individuals because the data for any one could be recorded in several different books. The 150 sampled persons underwent 1075 tests and Table 2 shows the types of test carried out. Of the 150 persons 69 were involved in more than one type of test. A total of 120 persons were involved in tests with chemicals and 72 with more than one chemical type. The median number of days on which tests were carried out on an individual was 2 (range 1–13). In this sample, more tests took place on Mondays than on any other day (Monday, \( n = 423 \); Tuesday, \( n = 176 \); Wednesday, \( n = 197 \); Thursday, \( n = 167 \); Friday, \( n = 99 \); Saturday, \( n = 8 \); Sunday, \( n = 5 \)). This reflects the number of baseline tests that were carried out on the first day of each visit, Monday being the most frequent day for new intakes.

There were 736 tests involving chemical agents: 102 were mustard sensitivity tests, 167 rubber mix

<table>
<thead>
<tr>
<th>Book type</th>
<th>Category</th>
<th>First date</th>
<th>Last date</th>
<th>( n )</th>
</tr>
</thead>
<tbody>
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<td>01/12/1997</td>
<td>10</td>
</tr>
<tr>
<td>Alphabetical list</td>
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<td>01/01/1983</td>
<td>4</td>
</tr>
<tr>
<td>Mustard tests</td>
<td>Experimental</td>
<td>01/06/1931</td>
<td>01/05/1978</td>
<td>7</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>Experimental</td>
<td>01/01/1934</td>
<td>01/05/1988</td>
<td>8</td>
</tr>
<tr>
<td>Chamber experiments</td>
<td>Experimental</td>
<td>01/10/1938</td>
<td>01/10/1954</td>
<td>10</td>
</tr>
<tr>
<td>Day book</td>
<td>Experimental</td>
<td>01/12/1938</td>
<td>01/05/1956</td>
<td>14</td>
</tr>
<tr>
<td>Physiological tests</td>
<td>Experimental</td>
<td>01/01/1952</td>
<td>01/12/1957</td>
<td>1</td>
</tr>
<tr>
<td>Observers’ workbook</td>
<td>Experimental</td>
<td>01/01/1956</td>
<td>01/01/1972</td>
<td>7</td>
</tr>
<tr>
<td>Psychological tests</td>
<td>Experimental</td>
<td>01/06/1960</td>
<td>01/10/1974</td>
<td>2</td>
</tr>
<tr>
<td>Notebook</td>
<td>Experimental</td>
<td>01/10/1966</td>
<td>01/11/1983</td>
<td>6</td>
</tr>
<tr>
<td>Official diary</td>
<td>Experimental</td>
<td>01/01/1972</td>
<td>01/01/1988</td>
<td>16</td>
</tr>
<tr>
<td>Rubber mix tests</td>
<td>Experimental</td>
<td>01/01/1974</td>
<td>01/07/1984</td>
<td>1</td>
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<tr>
<td>Human volunteer studies</td>
<td>Experimental</td>
<td>01/02/1979</td>
<td>30/01/1992</td>
<td>18</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>01/06/1931</td>
<td>30/01/1992</td>
<td>111</td>
</tr>
</tbody>
</table>
Fig. 1. Example pages from the Porton Down archive. (a) Dermal exposure in the 1940s to a liquid vesicant with results recorded on a semi-quantitative erythema and vesication scale, with the area of skin affected. (b) Exposure to a nerve agent in 1952 with results expressed in table form. (c) Diary format, 1973.

Fig. 2. Comparison of annual numbers of persons tested at Porton Down from the Ministry of Defence database and from contemporaneous annual reports and other documents.
patch tests and 118 tests of treatments. The most commonly tested group of chemical warfare agents in this sample was the vesicants (n = 103) followed by riot control agents (n = 89). There were 44 nerve agent tests, 11 with incapacitants and 5 with irritants. No tests involved exposure to lung-damaging agents, blood agents, choking agents, smokes, fuels and incendiary devices or herbicides. In this sample, a relatively large number of tests were classified as ‘other’ (n = 61). The non-chemical tests included chest X-rays, height and weight measurements and psychological profiling. There were 88 tests which could not be categorized solely from the information available in the books. Taken with the 36 tests involving unknown chemicals, 123 (11%) of the 1075 tests could not be adequately categorized using only the information in the books (Table 2).

The most commonly tested vesicant in this sample was sulphur mustard (82 of 103 vesicant tests). The median number of vesicant tests per person was 2 (Table 2). The commonly used method of vesicant testing involved placing several individual drops on the skin of the anterior surface of the forearm (Fig. 1a); we noted each drop as a separate test. Sarin was the most commonly tested nerve agent in this sample (37 of 44 nerve agent tests). The median number of nerve agent tests per person was 1. The lachrymator dibenz(b,f)(1,4)oxazepine (CR) was the most commonly tested riot control agent in this sample (56 of 89 riot control agent tests). The median number of tests per person of riot control agents was 2 and many were repeat tests of one substance at different concentrations. The median number of tests per veteran involving a treatment was 2; many involved repeat exposures to nerve agent prophylactic tablets; pyridostigmine (41 of 118 treatment tests) was the most commonly tested. In this sample, 52 (51%) tests involving vesicants took place in the 1940s, and 18 (41%) tests involving nerve agents. In all, 65 (73%) riot control tests took place in the 1970s. Most tests involving treatments took place in the 1970s (n = 49, 42%) or 1980s (n = 48, 41%).

Some information was found to be available on potential exposure or effect modifiers, depending on the type of agent under test and on the experimental circumstances. This information included the following: the presence or absence of a physical barrier (such as a textile), between the exposure and exposure site; exposure site; exposure state (whether solid, liquid or gas/vapour); respirator use; use of other protective equipment; whether the test took place in a chamber; and the use of decontaminants, prophylactics or antidotes. Exposure route (dermal, inhalation, etc.) could be imputed in many instances from the experimental circumstances.

### Availability of quantitative information on exposure

The availability of quantitative information on exposure in the tests is shown in Table 3. Overall, quantitative information on level of exposure was identified for 49% of tests, the best coverage being for vesicants (68%), treatment (67%) and nerve agents (66%). Level of exposure was documented in a range of units: drops (n), drop diameter (in millimetres), dilution (%), parts per billion, grams, milligrams, micrograms, cubic centimetres, milligrams per cubic metre and micrograms per litre. Chamber exposures to nerve agents were recorded as concentration × time in units of milligrams per cubic metre minutes. Duration of exposure (usually in minutes) was, overall, recorded in 31% of tests, but in 66% of vesicant tests and 77% of nerve agent tests. Mustard
sensitivity tests appeared to be standardized and it is understood that information on the test procedures and methodology is available in Porton Down documents, for example in Fairley (1932). Details of individual rubber mix compounds are also available.

**Availability of quantitative acute toxicity data**

Quantitative measures of acute toxicity were typically documented for vesicant (72%) and nerve agent (57%) tests, but not for agents in other categories (Table 3). The dermal effect of vesicant exposures was recorded on a semi-quantitative scale as the severity of erythema (reddening of the skin) and presence of vesication (blistering). Responses documented in this sample were: e−/C0, e−, e+, v. Our understanding is that e−/C0 represents mild reddening, e− reddening, e+ pronounced reddening and v the presence of a vesicle (blister) (Kingan, 1937). Quantitative responses to nerve agents were documented in two ways: change in pupil size and change in level of blood cholinesterase. The records also contained qualitative information about certain symptoms reported by some of the participants. As there were no plans to make use of qualitative symptoms data in the cohort study, none of this was abstracted for the sample.

**Exposures in the sample**

Information on level of exposure and duration of test to three selected substances (sulphur mustard, sarin and CR) by exposure route is shown in Table 4. Most (85% of 82) of the mustard tests were dermal with between 0.28 and 4000 μg of liquid mustard for between two and 360 min. In this sample, the test with the highest exposure concentration took place for 2 min and in the presence of a decontaminant. The exposure route most commonly documented for sarin was ‘mixed route’ (n = 25), a description we used for tests in a chamber where, as a result of the solubility and volatility of sarin, inhalation, ocular and dermal exposures were possible, although respirators were recorded as being worn in three tests. CR exposures in this sample were principally oral, part of a series of experiments to detect the lowest concentration at which food or water contaminated with CR could be detected.

**DISCUSSION**

These results are based on a sample of 150 veterans derived from a representative sample of 30 from each decade of the study period. Because of the sampling method used, the distribution of visits to Porton Down will not match that of the whole cohort and no inferences about exposures in the whole cohort can be made from these results. The most important finding of this study was that it will be possible to reconstruct exposures at an individual level for the cohort study from the records made available to us at Porton Down. Despite the 50-year period of the exposure records, the data quality appeared to be reasonably consistent over time. This exposure assessment will be a valuable component of the cohort study of mortality and cancer incidence in Porton Down veterans. The completeness of information is an important question in any historical cohort study (Enterline and Marsh, 1982); this study has provided evidence that the information provided to us appeared largely complete. It may be possible to undertake sensitivity analyses to estimate the effects of any missing data. Because many veterans had multiple tests, it was clear that it will be necessary to abstract data in a test-wise format and subsequently to link all tests for each person. A database has been designed for

<table>
<thead>
<tr>
<th>Chemical category</th>
<th>Number of tests in category</th>
<th>Information available on Level of exposure</th>
<th>Duration of exposure</th>
<th>Acute toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>n</td>
<td>Row %</td>
</tr>
<tr>
<td>Vesicant</td>
<td>103</td>
<td>70</td>
<td>68</td>
<td>68</td>
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<tr>
<td>Mustard sensitivity test</td>
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<td>100</td>
<td>102</td>
<td>100</td>
</tr>
<tr>
<td>Nerve agent</td>
<td>44</td>
<td>29</td>
<td>66</td>
<td>34</td>
</tr>
<tr>
<td>Riot control agent</td>
<td>89</td>
<td>44</td>
<td>49</td>
<td>8</td>
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<td>Incapacitant</td>
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<tr>
<td>Irritant</td>
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<td>3</td>
<td>60</td>
<td>3</td>
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<tr>
<td>Treatment</td>
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<td>Rubber mix test</td>
<td>167</td>
<td>n/a</td>
<td>—</td>
<td>n/a</td>
</tr>
<tr>
<td>Total</td>
<td>736</td>
<td>363</td>
<td>49</td>
<td>225</td>
</tr>
</tbody>
</table>

n/a = not available.

Table 3. Availability of quantitative exposure and acute toxicity data by chemical category in chemical tests identified for the sample of 150 persons.
the extraction of data for the exposure assessment (Fig. 3). Algorithms will be developed for data analysis using a hierarchical approach. At the first level above that of the cohort of veterans, it will be possible to classify each serviceman as ever/never exposed to any chemical at Porton Down. At the next level, it will be possible, for each serviceman and each chemical or group of chemicals, to define exposure as ever/never exposed. Mortality and cancer incidence will be studied within major exposure groupings. At the last level of complexity, it will be possible, for those exposed to vesicants or nerve agents, to define groups for analysis based on the level of exposure or the acute toxicity experienced. The exact measures of exposure and acute toxicity to be used will be decided after examination of all the available data.

For the majority of chemical tests recorded in the experimental books for this sample, the name of the chemical was clear and it could be assigned to a chemical warfare agent category derived from the NATO Handbook (US Department of the Army, 1996). However, in >10% of the tests undergone by this sample of servicemen, the chemical could not be categorized or the type of exposure was unclear. It may be that this percentage can be reduced in the exposure assessment by enquiries in the Porton Down library or to Porton Down staff.

In many occupational epidemiological studies the only information available which bears on exposure is job title and duration of employment and is, at best, semi-quantitative. For this cohort, in contrast, quantitative data on level and duration of exposure are available for vesicants and nerve agents, two of the largest subgroups of chemicals in this sample. Moreover, this quantitative exposure information is available for individuals in contrast with many occupational epidemiological studies where individual exposure can only be estimated from data relating to groups. Furthermore, the availability of acute toxicity data for vesicants and nerve agents offers potential for constructing a measure of absorbed dose, although it is as yet unclear if this measure of dose is relevant to mortality and cancer incidence. One challenge for the epidemiological analysis will be to classify veterans’ exposure using this quantitative information when the unit of measurement has changed over time, as is the case for both exposure and acute toxicity. The analysis will also need to consider sources of variation in these quantitative measurements, for example from difference in laboratory methods. For the measures of acute toxicity, such as change in level of blood cholinesterase, inter- and intra-individual variation in the response to exposure are also important (Brock and Brock, 1993).

The exposure and acute toxicity data for vesicants appeared to be in a similar format to that reported in the cohort study of WWII US Navy personnel exposed to sulphur mustard in human experiments (Bullman and Kang, 2000), raising the possibility of comparisons with this cohort.

This study allows some preliminary speculation about the levels of exposure received by the veterans who participated in these tests, although robust inferences on the whole range of exposures over 1939–1989 cannot be made from this study alone. While exposures have in some cases been high, leading to one fatality (Ministry of Defence, 2006), indications are that most were not. It is likely that these sub-lethal exposures are comparable to the sub-lethal exposures outside the immediate target zone in warfare or a terrorist incident, where a decreasing gradient of exposure from the point of release should be expected. Another similarity to warfare or a terrorist incident is that the exposures occurred as a single exposure of short duration or small number of short
Exposures from the UK chemical warfare programme

identifying details - all tests
- Book and page number
- Operator name and data entry date
- Veteran name and other identifying data (service number, rank)
- Date of test

Enter type of test
- Non chemical
- Rubber mix
- Mustard sensitivity

Enter presence of test only. No further data collected.

For all other chemical tests enter the following exposure information:
- Name of chemical/compound
- Exposure route
- Exposure state
- Respirator used?
- Clothing, protective clothing or other barrier?
- In chamber?

If not a vesicant or nerve agent, no further data collected.

If a vesicant or nerve agent enter the following additional exposure information:
- Site of exposure
- Quantity
- Duration
- Decontaminant used?
- Prophylactic used?
- Antidote used?
- Temperature used?
- Humidity

Acute toxicity information - vesicants
- Was skin reaction documented?
  - Severity of skin reaction

Acute toxicity information - nerve agents
- Pupil size before
- Pupil size after
- Cholinesterase before
- Cholinesterase after

If a vesicant or nerve agent, enter information on biological effect

Fig. 3. Diagram showing the decision path for entering data into the exposure database for the cohort study of Porton Down veterans.

... expose...cumulative exposures were, in general, low in this cohort over 1939–1989, then a very large study is likely to be needed to estimate any long-term health effects, including rarer outcomes such as specific types of cancer. The UK cohort includes ~20,000 veterans, although the numbers exposed to each specific chemical are lower.

Since much of the of the work at Porton Down appears to have been related to designing protection for UK forces against nuclear, chemical or biological attack, many of the exposures of test participants were modified by, for example protective clothing, barrier creams or pharmaceutical prophylaxis or antidotes. For example, in tests involving dermal vesicant exposures, the presence or absence of clothing, protective clothing or other barrier between the exposure and the skin was recorded. Although it will not be possible to transcribe every item written in the archive for use in the epidemiological study, it was clear that some information on potential exposure and effect modifiers can usefully be abstracted (Fig. 3).

Acknowledgements—We thank our colleagues at the University of Oxford for their contributions to this paper: Steven Allender, Sageet Amlani, Terence Boyle, Kate Brockhurst, Claire Brooks, Steve Davies, Chris Shield and Sue Walker. We thank Nick Blatchley, Dan King and Tracey Vennai from the Veterans Policy Unit of the Ministry of Defence (formerly the Gulf Veterans’ Illness Unit) and Gradon Carter, Hugh Dyson, Rick Hall, Marie Jones and Viv Worrall from the Defence Science and Technology Laboratory, Porton Down, who facilitated the work. We also thank the members of the Medical Research Council (MRC) liaison group for their helpful comments on the draft manuscript. The study was funded by a grant from the UK Ministry of Defence administered by the MRC (G0200288). The sponsors had no role in the collection, analysis or interpretation of data or in the writing of the report. No conflicting interests are declared. Ethical approval was granted...
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