<table>
<thead>
<tr>
<th>AD NUMBER</th>
<th>ADB955157</th>
</tr>
</thead>
<tbody>
<tr>
<td>LIMITATION CHANGES</td>
<td></td>
</tr>
<tr>
<td>TO:</td>
<td>Approved for public release; distribution is unlimited.</td>
</tr>
<tr>
<td>FROM:</td>
<td>Distribution authorized to DoD only; Critical Technology; 31 OCT 1983. Other requests shall be referred to Chemical Research and Development Center, ATTN: DRSMC-CLJ-IR, Aberdeen Proving Ground, MD 21010. This document contains export-controlled technical data.</td>
</tr>
<tr>
<td>AUTHORITY</td>
<td>ECBC memo dtd 15 Oct 2015</td>
</tr>
</tbody>
</table>

THIS PAGE IS UNCLASSIFIED
SIT: Lethal Concentration of Phosgene for Dogs for 7-1/2 Minute Exposure.

BY: W.H. Grossboek and E.J. Witherspoon.

DATE: January 22, 1922.
UNCLASSIFIED

LETHAL CONCENTRATION

OF

PROSOLVE

FOR

DOGS FOR 7-1/2 MINUTE EXPOSURE


Commander

Chemical Research and Development Center

ATTN: DRSMC-CLJ-IR

Aberdeen Proving Ground, MD 21010

W.M. GROSSBECK

and

M.C. WITHERSPOON.
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. INTRODUCTION</td>
<td>1</td>
</tr>
<tr>
<td>II. SUMMARY</td>
<td>1</td>
</tr>
<tr>
<td>III. CONCLUSIONS</td>
<td>1</td>
</tr>
<tr>
<td>IV. EXPERIMENTAL</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>4</td>
</tr>
<tr>
<td>V. CLINICAL HISTORY</td>
<td>4</td>
</tr>
<tr>
<td>VI. GROSS PATHOLOGY</td>
<td>5</td>
</tr>
<tr>
<td>VII. CONCLUSIONS</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>7</td>
</tr>
<tr>
<td>VIII. UNCOMPLETED AND FUTURE WORK</td>
<td>6</td>
</tr>
</tbody>
</table>
LETHAL CONCENTRATION OF PHOSGENE FOR DOGS FOR 7-1/2 MINUTE EXPOSURE.

January 23, 1922.

I. INTRODUCTION

The object of the present work was to determine the lethal concentration of phosgene for dogs for an exposure of seven and one-half minutes. The lethal concentration is defined as the least amount of the toxic substance in a gas-air mixture which will produce the deaths, within 10 days, of a majority (66-2/3%) of the animals exposed to a given concentration over a definite period of time. It is expressed in milligrams of compound per liter of air.

II. SUMMARY

The least concentration which will cause a majority of deaths within a period of 10 days lies between 1.08 and 1.15 milligrams per liter. The average concentration for the six dogs within the range indicated is 1.1 milligrams per liter.

III. CONCLUSIONS

The lethal concentration of phosgene for dogs after an exposure of 7-1/2 minutes may be placed at 1.1 milligrams per liter. This is the equivalent of 270.6 parts per million at 25°C. and 760 millimeters barometric pressure.

IV. EXPERIMENTAL

A. The apparatus used consisted of two electrically driven air pumps with an equalizing chain for steadying the constant flow of air, a mixing bulb in which the gas-air mixture was made and a large glass-sided box (inner dimensions 74.9 x 69.8 x 71.2 cm.) with a sliding front. This glass chamber was sealed air tight except at the point of entrance and exit of the gas-air mixture. The phosgene used was 99.6% pure.
b. Before dogs were placed in the chamber, concentrations were determined by preliminary runs. The flow of gas necessary to maintain these concentrations was noted and the run repeated with dog subjects. During the actual exposure of the dogs the concentration was again checked by chemical analysis of the gas-air mixture. Samples were aspirated from the chamber during exposure, absorbed in a suitable solvent and subsequently analyzed. The method of analysis was the modified Mohr method as assembled in brief by L. L. Satter in "Chemical Methods up to May 1918", Laboratory of the Pharmacological Division (Reference: P.H.S. Vol. V, No. 10).
### RESULTS OF EXPOSURES ON INDIVIDUAL DOG SUBJECTS

<table>
<thead>
<tr>
<th>Dog No.</th>
<th>Concentration (ppm/liter)</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>135</td>
<td>0.98</td>
<td>Died after 17 hours</td>
</tr>
<tr>
<td>146</td>
<td>1.05</td>
<td>Living after 10 days</td>
</tr>
<tr>
<td>119</td>
<td>1.08</td>
<td>Living after 10 days</td>
</tr>
<tr>
<td>153</td>
<td>1.08</td>
<td>Died after 6 hours</td>
</tr>
<tr>
<td>156</td>
<td>1.09</td>
<td>Died after 22 hours</td>
</tr>
<tr>
<td>180</td>
<td>1.1</td>
<td>Died after 18 hours</td>
</tr>
<tr>
<td>176</td>
<td>1.13</td>
<td>Living after 10 days</td>
</tr>
<tr>
<td>167</td>
<td>1.15</td>
<td>Died after 22 hours</td>
</tr>
<tr>
<td>177</td>
<td>1.17</td>
<td>Died after 10 hours</td>
</tr>
<tr>
<td>154</td>
<td>1.17</td>
<td>Died after 50 hours</td>
</tr>
<tr>
<td>179</td>
<td>1.16</td>
<td>Died after 16 hours</td>
</tr>
<tr>
<td>174</td>
<td>1.1</td>
<td>Died after 4 hours</td>
</tr>
<tr>
<td>178</td>
<td>1.22</td>
<td>Living after 10 days</td>
</tr>
<tr>
<td>129</td>
<td>1.23</td>
<td>Died after 56 hours</td>
</tr>
<tr>
<td>164</td>
<td>1.27</td>
<td>Died after 24 hours</td>
</tr>
<tr>
<td>172</td>
<td>1.3</td>
<td>Died after 19 hours</td>
</tr>
<tr>
<td>175</td>
<td>1.31</td>
<td>Died after 30 hours</td>
</tr>
<tr>
<td>152</td>
<td>1.35</td>
<td>Died after 82 hours</td>
</tr>
<tr>
<td>153</td>
<td>1.36</td>
<td>Living after 10 days</td>
</tr>
<tr>
<td>142</td>
<td>1.38</td>
<td>Died after 11 hours</td>
</tr>
<tr>
<td>171</td>
<td>1.4</td>
<td>Died after 57 hours</td>
</tr>
<tr>
<td>154</td>
<td>1.42</td>
<td>Died after 6 hours</td>
</tr>
</tbody>
</table>
0. RESULTS OF EXPOSURES ON INDIVIDUAL DOG SUBJECTS:

<table>
<thead>
<tr>
<th>Dog No.</th>
<th>Concentration</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>173</td>
<td>1.43</td>
<td>Died after 20-1/2 hours</td>
</tr>
<tr>
<td>112</td>
<td>1.52</td>
<td>Living after 10 days</td>
</tr>
<tr>
<td>115</td>
<td>2.11</td>
<td>Died after 16 hours</td>
</tr>
</tbody>
</table>

V. CLINICAL HISTORY:

A. During Exposure:

Irritation was evidenced by continuous blinking of the eyes, occasional sneezing and slight salivation. In some cases the dogs lachrymated after six minutes. Restlessness was manifested during the first minutes of exposure but in general the dogs remained quiet, awaiting release.

B. Following Exposure:

Following exposure the dogs were very quiet and slightly depressed in practically all cases. Their eyes remained open and were clear and normal in appearance. In a few cases, at the end of 12 to 16 hours, there was a slight watery discharge from the nose.

Immediately following exposure, respiration was fairly normal. Later it usually increased in rate, rising to as high as 40 to 44 in some cases. Furthermore it was irregular, and often audible. Coughing was noted in one dog. When dogs died within 6 to 12 hours the respiration soon became very shallow and remained so until death.

Immediately following exposure, the heart beat was regular, but within a few hours decreased in rate to as low as 64 in some cases. When the dogs died from 12 to 24 hours after exposure the rate seemed to increase to about normal or slightly above.
VI. GROSS PATHOLOGY:

The external examination of the dogs autopsied following exposure to phosgene gas revealed nothing abnormal. Generally speaking, the dogs were in good condition. The eyes were clear and the nose was free of fluid. In some cases, the mouth was found to contain a blood stained watery fluid. Occasionally this fluid had poured from the mouth and after death was found caked on the hair of the face.

Internally the following pathological changes were noted; the mucous membrane of the larynx and trachea in all cases was slightly injected, injection occurring between the cartilaginous rings. The lumen in all dogs was filled with an exudate which was either clear and mucoid or bloody and frothy in character. This exudate extended down into the bronchi. Further examination of the dogs showed that they may be classified into three classes according to the time of death:

1. Acute - dogs dying within 48 hours.
2. Sub-acute - dogs dying 3-1/2 to 10 days following exposure.
3. Chronic - dogs dying or killed after 10 days.

In the cases of acute deaths, upon removing the chest wall, a very striking picture was presented. The entire thoracic cavity was filled by the voluminous lungs which did not collapse upon touching them. In a few dogs the lungs practically concealed the heart. The color of the lungs was quite characteristic. They were purplish red with irregular bluish-white patches, giving them a decidedly mottled appearance. The purplish color was due to the extreme congestion of the vessels which was noticed immediately, while the bluish white areas were due to the emphysematous condition of the lungs. Generally speaking, the lungs were doughy and oedematous in consistency. In dogs dying within 6 hours after exposure, the emphysematous condition was not so marked while in those dying in 22-26 hours, it was very prominent. Upon cutting the lung a fluid exuded which was usually straw colored from the pale areas and bloody from the congested areas. The cut surface was generally smooth and regular, but in some cases, tiny grayish areas were seen and the smallest bronchioles stood out quite prominently due to the oedematous condition of their walls. Oedema was most marked in the lower lobes and emphysema in the upper and middle lobes. The emphysematous areas varied in size from small patches to areas involving practically the whole lobe. Emphysema was especially noted along the margins of the lungs. In about 40% of the dogs, a blood-stained fluid was present in the pleural cavity. The amount of fluid varied from 5 cc. to 150 cc. In this latter case, the lungs appeared drowned. In about 50% of
the dogs dying acutely, the right side of the heart was seen
to be noticeably dilated, and in a few dogs the left side was also
involved. The heart muscle and valves appeared normal however.
in three dogs, the vessels of the mediastinum seemed injected
and the mediastinal tissue oedematous. The abdominal viscera
appeared to be normal except in a few cases where there was some
evidence of a general splanchic congestion. The liver, how-
ever, seemed slightly darker and heavier than normal and was oc-
casionally bile stained in the region of the gall bladder.

In the group of sub-acute deaths, the lungs were
found to be voluminous and heavy. Oedema, congestion and en-
physesma were found. The surface generally was smooth, but in many
cases there were pale pink firm areas which stood out above the
rest of the puffy, crepitant lungs. In the dogs dying in three
to four days, these consolidated areas were less numerous than
in the more delayed deaths. These areas of consolidation were
found principally near the margins of the lungs. Upon cutting
the lungs and examining the bronchioles from above downward they
were found to become progressively more dilated and inflamed.
Many were seen to be filled with plugs of exudate. Their walls
also appeared thickened, so that on section they were very promi-
nent. This exudate was frequently of a mucous purulent nature,
but occasionally was straw colored and clear. Oedema was especially
marked around the larger vessels. The posterior and lower parts
of the lungs were frequently heavy and consolidated and presented
a pneumonic appearance. The heart was dilated as in the acute
deaths and again approximately the same conditions were found in the
abdominal viscera.

If dogs survived more than 10 days and were then killed,
the following conditions were found: the upper air passages were
unaffected. The most marked change in the lungs was the presence
of oedema. Emphysema was also found but was not so prominent a
feature as the oedema. The bronchioles were seen to be affected
but were apparently in a state of repair from the previous inflam-
matory condition.

VII. CONCLUSIONS:

A. Lethal Concentration:

A condensation of the results of exposures on indi-
vidual dogs gives the following table, from which the lethal con-
centration may be derived.
From this table the least concentration which will cause a majority of deaths within 10 days is seen to lie between 1.08 and 1.15 milligrams per liter. The average concentration for the six exposures made within the range indicated is 1.1 milligrams per liter.

The lethal concentration of phosgene for a 7-1/2 minute exposure of dogs may be placed, therefore, at 1.1 milligrams per liter or 270.6 parts per million at 25°C. and 760 millimeters pressure.

B. Clinical History:

Phosgene acts as a respiratory irritant. The chief effects shown are the changes in respiration and pulse, showing the effect of the gas on the heart and lungs. Dogs dying shortly after exposure, are quiet but show shallow, rapid respiration and increased pulse. In dogs which survive for 3 to 10 days, respiration and pulse tend to return to normal until shortly before death, when the respiration decreases to a very low rate.

C. Gross Pathology:

When death is acute, the main changes are confined to the heart and lungs. The lungs are intensely congested and edematous.
Dilatation, congestion and plugging of the bronchioles with exudate cause the emphysematous condition seen over the entire lung. The obstruction of the capillaries leads to the dilatation of the heart which is characteristic of this stage.

When death is delayed, death results from infection of the lungs. The upper air passages are unaffected but there is an extensive infection and some destruction of the bronchioles. The entire lung substance may be involved in this infection as seen by the pneumonic condition when the lung is cut. Death is usually due to pneumonia.

When dogs die or are killed during the chronic stage of phosgene poisoning, oedema of the lungs is the most noticeable pathological change. The heart at this stage appears to be normal.

VIII. UNCOMPLETED AND FUTURE WORK:

Macroscopic studies only have been completed on the present series of dogs. At the time of autopsy sections of heart, lungs, liver, kidneys, spleen and pancreas were preserved. Sections of these were made but microscopic studies of the slides have not been completed. A future report will cover this work.

The determination of the lethal concentration of phosgene for a 7-1/2 minute exposure is a part of a larger problem for plotting a complete lethal curve from 15 seconds to several hours exposure. The present report, therefore, is a part of a future presentation of the lethal data of phosgene.
SUBMITTED BY:

A.R. Young

M.G. Witherspoon

William M. Groesbeck
In Charge, Control Section.

A.R. Koontz, M.D.
In Charge, Pathological Section

Authors:

W.M. Groesbeck and
M.G. Witherspoon

SUPervised by:

Harry A. Kuhn,
1st Lieut., C.W.S., U.S.A.,
Chief, Dept. of Toxicology.

APPROVED BY:

D.B. Bradner,
Chief, Chemical Division.

Report on Lethal Concentration of Phosgene
for Dogs for 7-1/2
Minute Exposure.

Copied:  mcg)  
8 copies made)  - 9 -
MEMORANDUM THRU Director, Edgewood Chemical Biological Center, (RDCB-D/Dr. Joseph Corriveau), 5183 Blackhawk Road, Aberdeen Proving Ground, Maryland 21010-5424

FOR Defense Technical Information Center, 8725 John J. Kingman Road, Ft Belvoir, VA 22060

SUBJECT: Internal Request for Change in Distribution

1. This action is in response to an Edgewood Chemical Biological Center (ECBC) Internal Request for a Change in Distribution for the following documents as listed in attachment.

2. The listed documents have been reviewed by ECBC Subject Matter Experts and deemed suitable for the change in distribution to read “Approved for public release; distribution unlimited.”

3. The point of contact is Adana Eilo, ECBC Security Specialist, (410) 436-2063 or adana.l.eilo.civ@mail.mil.

Encl

RONALD L. STAFFORD
Security Manager
PHOSGENE REFERENCES


