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EDGEWOOD ARSENAL, EDGEWOOD, MD.
MAJOR E.J. ATKISSON, COMMANDING.

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C. E. Otto. REPORT NO. E.A.C.D. 101, COPY NO. 1.
Lt. Col., C.W.S. PROJECT NO. A 3.1

SUBJECT: Lethal Concentration of
Phosgene for Dogs for
7-1/2 Minute Exposure.

J.E. MILLS, TECHNICAL DIRECTOR.

BY: W.M. Groesbeck and
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D.B. BRADNER, CHIEF, CHEMICAL DIVISION.

DATE: January 23, 1922.

EACD 101

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LETHAL CONCENTRATION

OF

PROGGER

FOR

DOGS FOR 7-1/2 MINUTE EXPOSURE

January 23, 1922.

Commander *W.D. only: 67*
Chemical Research and Development Center
ATTN: DRSMC-CLJ-IR
Aberdeen Proving Ground, MD 21010

BY:

W.M. GROESBECK

and

M.G. WITHERSPOON.

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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 99.8% 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. Sattler in "Chemical Methods up to May 1918", Laboratory of the Pharmacological Division (Reference: P.R.S. Vol. V, No. 210).

C. RESULTS OF EXPOSURES ON INDIVIDUAL DOG SUBJECTS:

Dog No.	Concentration Mgm/liter	Results
135	0.98	Died after 17 hours
146	1.05	Living after 10 days
119	1.08	Living after 10 days
153	1.08	Died after 6 hours
156	1.09	Died after 22 hours
180	1.1	Died after 18 hours
176	1.13	Living after 10 days
167	1.15	Died after 22 hours
177	1.17	Died after 10 hours
154	1.17	Died after 50 hours
179	1.18	Died after 16 hours
174	1.2	Died after 4 hours
178	1.22	Living after 10 days
120	1.23	Died after 36 hours
164	1.27	Died after 24 hours
172	1.3	Died after 19 hours
175	1.31	Died after 30 hours
152	1.36	Died after 82 hours
133	1.36	Living after 10 days
142	1.38	Died after 11 hours.
171	1.4	Died after 57 hours
134	1.42	Died after 6 hours

C. RESULTS OF EXPOSURES ON INDIVIDUAL DOG SUBJECTS:

Dog No.	Concentration mgms/liter	Results
173	1.43	Died after 20-1/2 hours
112	1.52	Living after 10 days
115	2.11	Died after 16 hours

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 splanchnic congestion. The liver, however, seemed slightly darker and heavier than normal and was occasionally 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 emphysema 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 prominent. This exudate was frequently of a muco-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 inflammatory condition.

VII. CONCLUSIONS:

A. Lethal Concentration:

A condensation of the results of exposures on individual dogs gives the following table, from which the lethal concentration may be derived.

Conc. mgm/l from - to	Deaths in 24 hours	Deaths between 24-48 hrs.	Deaths between 2-10 days	Total Deaths	Total per- cent deaths 10 days
1.52 - 2.11	1/2	-	-	1/2	50
1.38 - 1.43	3/4	-	1/4	4/4	100
1.27 - 1.36	2/5	1/5	1/5	4/5	80
1.17 - 1.23	3/6	1/6	1/6	5/6	83-1/3
1.08 - 1.15	4/6	-	-	4/6	66-2/3
0.98 - 1.05	1/2	-	-	1/2	50

Numerator - Number of dogs died

Denominator - Number of dogs exposed

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 congest^{ed} and oedematous.

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.

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

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US ARMY RESEARCH, DEVELOPMENT AND ENGINEERING COMMAND
EDGEWOOD CHEMICAL BIOLOGICAL CENTER
5183 BLACKHAWK ROAD
ABERDEEN PROVING GROUND, MD 21010-5424

REPLY TO
ATTENTION OF

RDCB-DPC-RS

15 October 2015

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

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Encl


RONALD L. STAFFORD
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