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WAR DEPARTMENT.
CHEMICAL WARFARE SERVICE,
EDGEWOOD ARSENAL, EDGEWOOD, MD.
COLONEL C. W. EXTON, COMMANDING.

Lieut. Col. E. B. Vedder, M.C.,
Chief, Medical Research Division.

Lieut.Comdr. D.C.Walton, M.C.,
Chief, Dept. of Toxicology.

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PROJECT NO. A3.5-3.

SUBJECT: The Toxicity of Hydrocyanic Acid Gas on Dogs, Monkeys, Mice, GUINEA PIGS AND RABBITS

BY: G.C.Armstrong
A.R.Koontz
M.G.Witherspoon.

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THE TOXICITY OF HYDROCYANIC ACID GAS ON DOGS, MONKEYS, MICE, GUINEA PIGS AND RABBITS.

by

G.C.Armstrong
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THE TOXICITY OF HYDROCYANIC ACID GAS ON DOGS, MONKEYS, MICE, GUINEA PIGS AND RABBITS.

ABSTRACT

This report treats of the toxicity of hydrocyanic acid gas on various animals for varying short lengths of exposure. The mode of action, symptoms, pathology and a review of British and German toxicity figures are also briefly discussed.

TOXICITY.

1. Dogs.

a.	30	second exposure of dogs	1.49 mg/l
b.	60	" " " "	0.67 "
c.	180	" " " "	0.34 "
d.	450	" " " "	0.208 "

2. Monkeys.

a.	30	second exposure of monkeys	1.68 mg/l
b.	60	" " " "	0.77 "
c.	180	" " " "	0.58 "
d.	450	" " " "	0.30 "

3. Mice.

a.	30	second exposure of mice	0.77 mg/l
b.	60	" " " "	0.567 "
c.	180	" " " "	0.367 "
d.	450	" " " "	0.242 "
e.	600	" " " "	0.190 "

4. Guinea pigs.

a.	30	second exposure of guinea pigs	2.53 mg/l
b.	60	" " " " "	1.64 "
c.	180	" " " " "	0.812 "
d.	450	" " " " "	0.35 "

5. Rabbits.

a.	30	second exposure of rabbits	1.48 mg/l
b.	60	" " " "	0.785 "
c.	180	" " " "	0.464 "
d.	450	" " " "	0.25 "

THE TOXICITY OF HYDROCYANIC ACID GAS ON DOGS, MONKEYS, MICE, GUINEA PIGS AND RABBITS.

I. INTRODUCTION.

The object of this work was to determine the lethal concentration of HCN on dogs, monkeys, mice, rabbits and guinea pigs for the following times of exposure: 30 seconds, 60 seconds, 180 seconds and 450 seconds.

II. EFFECTS ON TISSUES AND BODY FUNCTIONS.

Hydrocyanic acid and the cyanides have long been recognized as violent poisons which act very quickly. For this reason and also as their action is easy to study a great deal of work has been done on them. The following remarks, briefed from many sources, reflect the consensus of present day opinions on cyanides and hydrocyanic acid.

The majority of the cyanides are toxic in proportion to the amount of CN they contain. As potassium cyanide and sodium cyanide are more easily handled than hydrocyanic acid gas they are the compounds usually fed or injected intravenously in laboratory experiments. As a result of such experiments Sollmann in his Manual of Pharmacology summarizes the action of HCN as follows, "Hydrocyanic acid is probably the most rapidly acting poison. It produces death under asphyxial symptoms, by hindering the oxidative processes of the tissues. It also interferes with most other fermentations and is therefore a general protoplasmic poison. Compounds containing the CN radicals are toxic only if they can liberate HCN. Ferro-, ferri-, and sulphocyanides are stable and therefore do not show these effects. When given in doses small enough to permit of watching its action, this is seen to consist in a fleeting stimulation of certain parts of the central nervous system, followed by depression and paralysis. The action begins in the medulla. The vomiting, respiratory, vagus, pupil-dilator, and vasomotor centers are all stimulated. Then comes unconsciousness, and after this convulsions. In man these are probably mainly, medullary in origin. Then follows paralysis of the whole central nervous system. Involuntary evacuations of feces, urine, and semen are frequent."

Effects on special tissues and functions.

1. The blood. The cyanide does not combine with the haemoglobin. Cyan-haemoglobin and cyan-oxyhaemoglobin are only formed after several hours exposure and with difficulty. The small trace formed can only be due to laking of the corpuscles; intact red cells will not take up CN. We have been unable to demonstrate cyanogen in the blood of our animals, even on using a large amount and distilling it, and it is reasonable to presume that it is not present in any detectable quantity. The bright color of the blood in poisoning is due to the fact that the venous blood contains an excess of oxygen over the normal. In other words the tissues have been unable to remove the oxygen from the blood. The oxygen in the blood is more readily dissociated than in the normal. This is due to a diminution of the alkali reserve which accompanies the anoxaemic formation of fixed acid and in cyanide poisoning the blood has been shown to contain a slight excess of fixed acid. This acid, lactic acid, has been found both in the blood and urine of animals poisoned by HCN.

2. The blood-vessels. There is an early rise of the blood pressure due partly to central stimulation and partly to an increased out pouring of secretion from the suprarenal glands. This initial rise is soon followed by a marked fall due to vaso-motor paralysis and also to direct action of CN on the vessel walls. The weakening of the heart beat due to oxygen lack and direct action of the poison also contributes largely to the fall in blood pressure.

3. Heart. In low concentrations cyanides do not affect the isolated heart greatly. With stronger solutions a weakening of the force of contractions is seen, also an alternation of beats and finally a heart-block similar to that seen in asphyxia. In injected animals a similar effect is seen - first a slowing of the beats due in the early stages to central vagal stimulation and in the later stages to heart-block.

4. Respiration. Small doses whether by inhalation or injection cause quicker and deeper respirations. Later the respirations become slower and shallower, with prolonged pauses (Cheyne-Stokes type). The above changes are caused by a primary stimulation followed by a later paralysis of the respiratory center. With large doses the immediate cause of death is this respiratory paralysis as the heart continues to beat after respirations have ceased. The gas is not irritant to the lungs and the above effects on the respiration occur in vagotomized dogs.

5. Muscle tissue. Cyanides have a marked effect on plain muscle, causing the rhythmic motions of isolated intestinal loops to cease. In low concentrations there is no marked effect on striped muscles other than a slowing of the rate of recovery from fatigue. Stronger concentrations cause immediate death of the tissue but this effect is never seen in poisoning cases.

6. Nervous system. The central nervous system is first stimulated and then depressed. The spinal cord centers are affected less and recover first. The main action is on the medulla oblongata and lower brain. The inhibitory influence on the respiratory center is marked from the first, but later the whole central nervous system is paralyzed. The early convulsions are due to a direct stimulating effect on the higher centers, the later ones are probably asphyxial in origin.

7. Action on ferments. In general cyanides have a marked influence on ferments and the lower forms of life, inhibiting such varied phenomena as the action of blood on hydrogen peroxide, the activity of platinum sponge black, the growth of yeasts and plants and the germination of seeds.

8. Excretion. A certain amount is excreted by the lungs. The remainder is excreted as sulphocyanides after being bound in the body to sulphur containing molecules.

Theories of action. The action of hydrocyanic acid on the tissues as noted above is practically the same as that of asphyxia. The marked difference between the two conditions is the presence of an excess of oxygen in the blood in cyanide poisoning. The tissues are suffering from lack of oxygen but it is an internal asphyxia, undergone in the presence of an abundance of oxygen which they cannot utilize. This failure to utilize the oxygen may be due

1. To the HCN inactivating the oxygen.
2. To an effect on the intracellular enzymes generally.
3. Most probably of all, to a chemical action on some part of the oxidase system, probably the autoxidisable substances. These contain SH and cyanogen is excreted as sulphocyanates.

While the general tendency is to ascribe the whole effect of the cyanides to their action on the oxidation processes, the immediate inhibition of the respiratory center by doses that do not greatly affect the oxidative processes in other organs suggests that hydrocyanic acid may have a specific action on this center.

Lethal dose. This is usually given as 0.05 gram of absolute HCN for man. The lethal dose by respiration is usually believed to be less than the above and our figures confirm this view.

III. BRITISH AND GERMAN TOXICITY BY INHALATION FIGURES.

A. The figures obtained by the British observers during the late war follow. The graphs referred to are not included this being considered unnecessary.

C.P. 2989.

Lt.Colonel Crossley.

Annexed is a report showing the lethal doses of A.C. to animals,etc. Similar statistics for unconsciousness are as yet incomplete. They indicate that about half the time of lethal exposure is necessary to cause unconsciousness, except at high concentrations, when the margin between the two is very slight.

10-12-17. (Signed) J. Barcroft.

REPORT
on
TOXICITY OF HYDROCYANIC IN ANIMALS.

The following data give the lethal dose of A.C. for monkeys, goats, dogs, cats, rabbits and rats respectively. The results are given in tabular form and also as graphs, the key to which is as follows:-

Ordinate left side, concentration in volume of air which contains one volume of the gas.
" right side. ditto in mgrms. per litre.
Abscissa time in minutes for which the animal was exposed to the gas. None of these figures go beyond one hour.

X = Animal died subsequently.)
O = Animal survived.) Porton experiment.
T = (Cats) Animals died in Prof. Cushney's experiments.
H = (Rabbits) Animals died in Miss Dufton's experiments.

A comparison of the curves for the six species of animals enumerated above shows a great difference in their susceptibilities to A.C. as regards:-

(i) The time which lethal doses take to act upon the animal.
(ii) The minimal dose which is lethal, however long the animal is exposed to it.

The most interesting feature of these diagrams is the comparison between the dog, on the one hand, and the goat and monkey, on the other. The dog is the most susceptible of the animals tested, the goat and the monkey do not differ greatly and are the least susceptible. The goat, in size, and the monkey, in species, are the animals most akin to man in the series. Whether, therefore, on the argument of size, or the much stronger one of species, there seemed to be good reason for the supposition that for a given dose at least three times the exposure was necessary for man as for the dog, and similarly for a given exposure in time, a comparatively small dose would kill a dog.

Indeed, the argument seemed so clear, and the decision so important, that there was little excuse for avoiding the direct issue between man and dog.

One observer and one dog were, therefore, exposed simultaneously, without protection, to an atmosphere of 1/2000 A.C., with the object of comparing the relative effects of the gas on each. The experiment ran the following course:

Time from zero.	Dog.	Man.
50 seconds.	Became unsteady.	----------
1 min. 15 secs.	On floor unconscious.	----------
1 min. 30 secs.	Crying sounds and tetanic convulsions sufficiently established to render it probable that the animal was in extremis--------	
1 min. 31 secs.	----------	Came out of chamber and put on respirator, having felt no symptoms.
1 min. 33 secs.	Pulled out by lead.	----------
5 minutes.	----------	Slight momentary feeling of nausea.
10 minutes.	----------	Attention difficult to concentrate in close conversation.

Direct experiment, therefore, leaves no doubt that the dog is of quite a higher order of susceptibility to A.C. than is man.

10-12-17. (Signed) Joseph Barcroft.

The observer mentioned in this report was Mr. Barcroft.

(Signed) Arthur W. Crossley.

C.R.Young
Sec
-4 Jan 1918

Deaths

TABLES SHOWING Total Exposures OF ANIMALS in A.C.

MONKEYS

CONCENTRATION M'grms per Litre	Vol. of air containing 1 Vol. of AC	TIME OF EXPOSURE ½'	1'	2'	3'	5'	6'	10'	15'	20'	30'	45'	60'
1.2	1,000			0/2	1/2								
0.86	1,400				1/2								
0.75	1,600					2/2							
0.60	2,000			0/2			0/2	1/2			1/1		
0.40	3,000				0/3								
0.35	3,400									0/2			
0.24	5,000										1/3		
0.20	6,000											3/3	
0.18	6,800										1/3		
0.12	10,000											0/8	

GOATS

CONCENTRATION M'grms per Litre	Vol. of air containing 1 Vol. of AC	1'	2'	3'	5'	6'	10'	15'	20'	30'	45'	60'	120'	240'
1.7	709			1/1										
1.2	1,000			3/4										
0.91	1,320			1/1										
0.86	1,400			1/3										
0.71	1,700			0/1										
0.67	1,800						4/4							
0.60	2,000					1/3								
0.48	2,500				0/4		3/4		3/4					
0.36	3,350							1/4	7/8					
0.30	4,000									4/4				
0.24	5,000							0/4		3/4		4/8		
0.18	6,800											0/4	0/4	
0.12	10,000													0/4

Deaths
TABLES SHOWING Total Exposures OF ANIMALS in A.C.

DOGS

CONCENTRATION M'grms per Litre	Vol. of air containing 1 Vol. of AC	½'	1'	1½'	2'	3'	5'	10'	15'	20'	30'	45'	60'
1.2	1,000	0/2	2/2										
0.60	2,000		2/2	0/1									
0.40	3,000					2/2							
0.24	5,000						0/3	2/3	2/2				
0.12	10,000							0/2					
0.11	11,000								1/2		2/2		
0.08	15,000										0/2		0/4
0.06	20,000												0/9

RATS

CONCENTRATION M'grms per Litre	Vol. of air containing 1 Vol. of AC	½'	1'	2'	3'	5'	7'	10'	15'	20'	30'	45'	60'
1.2	1,000		4/6	4/6	12/12								
0.60	2,000		1/6		3/6		6/6						
0.40	3,000				1/6								
0.24	5,000								3/12		6/6		
0.18	6,800												1/6
0.12	10,000										4/12	5/6	3/6
0.06	20,000												1/12

Deaths

TABLES SHOWING Total Exposures OF ANIMALS in A.C.

RABBITS

CONCENTRATION M'grms per Litre	Vol. of air containing 1 Vol. of AC	½'	1'	2'	3'	4'	5'	7'	10'	15'	20'	30'	45'	60'
1.2	1,000		2/2		4/4									
0.86	1,400		1/2											
0.60	2,000				3/4				4/4					
0.40	3,000				1/2									
0.35	3,400								3/4					
0.24	5,000									3/7		0/4		
0.18	6,800													2/4
0.12	10,000													0/2
Miss Dufton's Experiments														
0.67	1,800			2/2					7/8					
0.48	2,500			2/3		5/9		1/2						
0.34	3,500			0/1		0/1		0/1	0/3					
0.30	4,000			0/1		0/3		0/1	1/2					

Deaths

TABLES SHOWING Total Exposures OF ANIMALS in A.C.

CATS

CONCENTRATION M'grms per Litre	Vol. of air containing 1 Vol. of AC	½'	1'	2'	3'	5'	7'	10'	15'	20'	30'	45'	60'
1.7	709				1/1								
1.2	1,000		2/3	2/2	3/3								
0.86	1,400		2/2										
0.71	1,700		1/2										
0.60	2,000				3/3			3/3					
0.40	3,000				0/2								
0.35	3,400							4/4					
0.24	5,000					2/3		3/3	3/3		3/3		
0.20	6,000							1/2	1/2				
0.18	6,800												2/5
0.12	10,000										0/3		0/4
Prof. Cushney's Experiments													
0.75	1,600				2/2								
0.60	2,000				1/2								
0.44	2,700				0/2								
0.20	6,000				0/2								

B. German Figures. These were obtained from an article by Flury and W. Heubner in the Biochemische Zeitschrift, Vol. 95, Nos. 3 and 4. They make the following statements. Cats can inhale a concentration of 0.1 mg/l for one half to three quarters of an hour without death. In these animals the maximum effect is noted in from 5 to 15 minutes, the animal lying unconscious and breathing spasmodically with slight convulsions from time to time. These animals usually improve after removal from the gas but in some cases death may occur after several hours. Concentrations over 0.35 mg/l are at once fatal to cats, respirations ceasing in 2 minutes. A concentration of 0.04 mg/l to 0.05 mg/l was found to be permanently ineffective by Lehmann but 0.06 mg/l to 0.07 mg/l was found to have a toxic effect and was generally fatal after an exposure of several hours.

Flury, as opposed to the British, considers man to have the same susceptibility to poisoning by inhalation as the dog or the cat. He bases this view on the following experiment carried out on monkeys.

In a gas chamber of 12 cubic metres capacity a medium sized Malay macaque, a dog and a cat were placed. The concentration was 0.14 mg/l maintained by continuous flow method and checked by analysis of the gas air mixture. As soon as the dog and monkey were overcome they were removed. The cat remained 7 minutes more, unconscious but breathing.

The results were as follows:

Species	First indication of poisoning.	First indication of symptoms of paralysis of functions.	Beginning of serious general crippling of functions.	Recovery after beginning of experiment.
Monkey	After 4 min. yawning indication of nausea. After 6 min. vomiting and coughing.	After 8 min. the animal staggered and collapsed.	After 12 min. convulsions, heavier breathing assumption of position on side.	After 19 min. improved resp. After 21 min. spontaneous movements began again.
Dog	After 3 min. nausea choking, after 5 min. vomiting.	After 9 min. ataxia and reeling.	After 10 min. convulsions, heavy breathing side position.	Reflexes again appear at end of 20 min.
Cat	After 3 min. choking- after 5 min. vomiting.	After 6 min. dyspnea and side position.	After 6 to 7 min.	After 28 min. beginning of spontaneous movements.

All three animals recovered completely. In a further experiment with a green long tailed monkey the results corresponded to those above.

Flury concludes that the dog and monkey have a resistance power similar to that of the cat but less than the rabbit and the smaller rodents.

IV. EXPERIMENTAL.

A. Material. The HCN was furnished by the Chemical Division of Edgewood Arsenal. An analysis by the Analytical Department of Edgewood Arsenal gave a water content of 3%.

The containers were large 150 pound cylinders and were kept in the brine room of the ice plant at all times.

The Wolff bottle containing the sample for immediate use was kept in cold storage room of the Toxicological Laboratory when not in actual use.

The liquid HCN when first drawn from the cylinder was a clear water white but rapidly changed to a greenish color in the case of the first sample used. Succeeding samples were a bright pink in color.

B. Apparatus and Manipulation.

1. Apparatus. The description of the continuous flow chamber apparatus with photostats may be found in report #15 E.A.M.R.D. with the following corrections:

The gas was removed from the metal cylinder and placed in an eight liter Wolff bottle with two openings. A bubbler was inserted in the liquid HCN and connected to a pressure pump by rubber tubing. Between the pump and liquid gas two equalizing bottles were used to steady the flow of air, also a flowmeter to measure the amount of air passed through the gas. The Wolff bottle was connected to the gas air line C' at F with rubber and glass tubing.

2. Manipulation. The Wolff bottle containing the HCN was kept in an ice bath at 4°C for the 60, 180, and 450 second runs. It was found on the 30 second run that it was unnecessary to use ice in order to get the desired concentration. Blanks were run first and a point taken on the flowmeter that gave the desired concentration. The run was then repeated with an animal in the chamber.

During each exposure of an animal samples were drawn from the gas air line C' at G by means of an aspirating bottle and the result titrated.

30	second	run	½	liter	samples	were taken.
60	"	"	1	"	"	" "
180	"	"	2	"	"	" "
450	"	"	5	"	"	" "

In this way the actual concentration that the animal was exposed to was calculated.

Checks were made simultaneously of concentrations of the gas air mixture before entering and immediately after leaving the cage. In each case they were found to be the same. Thereafter, for convenience, all samples were taken from the ducts before entering the cage.

C. Method of Analysis. The sample of the air gas mixture was absorbed in 2% solution of sodium bicarbonate contained in two petticoat bubblers. Twenty-five cc of this solution were measured into each bubbler.

It was found that 50 cc of sodium bicarbonate solution was sufficient to collect all of the gas in the concentrations herein recorded.

The sample was washed from the bubblers into a beaker. Two cc of a 5% starch indicator and 10 cc of a 10% potassium iodide solution were added. The sample was then titrated with a N/100 iodine solution until a permanent blue color was reached. From the amount of iodine consumed the concentration in milligrams per liter was obtained.

$$\text{Calculation} - \frac{\text{cc of iodine} \times N \times .135}{\text{number liter sample}} = \text{milligrams per liter}$$

The N/100 iodine solution was standarized against a standard N/100 arsenic trioxide solution each day before exposing the animals. The 5% starch indicator and the 10% potassium iodide solutions were always freshly prepared.

D. Subjects. There was a wide variation in the type and condition of dogs used. This no doubt had a direct bearing on the results and introduced an error that could not be avoided.

Monkeys were not available in sufficient number to determine an accurate lethal point. The figures therefore on these animals can only be considered as approximate.

Animals used:	Dogs - - - - -	94
	Monkeys - - -	10
	Guinea pigs- -	22
	Mice - - - - -	205
	Rabbits - - -	17
	Canary - - - -	1

E. Selection of Lethal Point. The lethal concentration is defined in terms of milligrams per liter of the gas air mixture and is taken as the minimum concentration that will produce 60% of deaths. As the delayed deaths were due to hydrocyanic acid (no marked lesions being demonstrable at autopsy and the animals being in a stuporous paralyzed condition up to the time of death) they are included among the fatalities. This is contrary to the usual practice with such gases as chlorine, phosgene, etc., where only 48 hour deaths are recorded, later deaths being due to an intercurrent infection of the damaged lung.

Owing to a shortage of monkeys, rabbits and guinea pigs lethal points were selected as being between certain points as seen in the following tables.

30 SECOND EXPOSURE.

The data from which the minimum lethal concentration for 30 seconds was derived are tabulated herewith:

Dog Number	Collapse in Seconds	Concentration	Results	
1416	45	0.87	Recovered	
1415	60	0.92	Recovered	1/6*
1414	45	0.96	Recovered	Av.conc.
1422		1.07	Recovered	1.00
1418		1.10	Recovered	
1424	35	1.11	Died 9 days	
1423		1.15	Recovered	
1425	45	1.15	Recovered	2/5*
1419		1.28	Died at exposure	Av.conc.
1420		1.28	Died at exposure	1.23
1426	40	1.30	Recovered	
1433	40	1.404	Died 3 days	
1442	40	1.43	Recovered	3/5*
1443	35	1.52	Died at exposure	Av.conc.
1444	30	1.53	Recovered	1.49
1448	35	1.57	Died 3 days	
1447		1.64	Recovered	
1449	35	1.65	Died 4 hrs.	3/5*
1446	35	1.66	Died 3 days	Av.Conc.
1452		1.76	Recovered	1.69
1375-A	35	1.768	Died 4 days	
1359-A	35	1.782	Died 5 days	
1365-A	55	1.835	Recovered	2/5*
1451	42	1.85	Recovered	Av.conc.
1458	37	1.93	Recovered	1.86
1392-A	35	1.94	Died 5 days	
1456	25	2.03	Died at exposure	
1454	30	2.08	Died at exposure	4/4*
1455	35	2.181	Died at exposure	Av.conc.
1411-A	28	2.314	Died at Exposure	2.15

* The numerator indicates the number of deaths and denominator shows number of dogs used.

The minimal lethal concentration for 30 seconds is placed at 1.49 milligrams per liter.

1 MINUTE EXPOSURE.

The data from which the minimum lethal concentration for 1 minute was derived are tabulated herewith:

Dog Number	Collapse in seconds	Concentration	Result	
1453		0.53	Recovered	)
1413	55	0.53	Recovered	)
1417	50	0.65	Died 60 hours	)
1421	53	0.67	Recovered	) 3/5*
1403	95	0.68	Recovered	) Av.conc.
1396	40	0.675	Died at exposure	) 0.670
1410	45	0.675	Died 12 hours	)
1408	45	0.69	Died at exposure	)
1409	70	0.69	Recovered	) 4/5*
1404	35	0.702	Died at exposure	) Av.conc.
1412	45	0.71	Died 12 hours	) 0.70
1402	47	0.71	Died 52 hours	)
1400	40	0.715	Died at exposure	)
1411	40	0.729	Recovered	) 3/5*
1406	70	0.729	Recovered	) Av.conc.
1401	55	0.742	Died at exposure	) 0.73
1399	55	0.742	Died at exposure	)
1374	38	0.77	Died 12 hours	)
1405	50	0.81	Died at exposure	) 3/5*
1390	50	0.824	Died at exposure	) Av.conc.
1375	55	0.824	Recovered	) 0.81
1392	80	0.844	Recovered	)
1394	50	0.844	Died at exposure	)
1393	37	0.85	Died at exposure	) 6/6*
1389	30	0.857	Died at exposure	) Av.conc.
1391	33	0.864	Died at exposure	) 0.889
1376	42	0.93	Died at exposure	)
1377	43	0.99	Died at exposure	)

* The numerator indicates the number of deaths and denominator shows number of dogs used.

The minimal lethal concentration for 60 seconds is placed at 0.67 milligrams per liter.

3 MINUTE EXPOSURE.

The data from which the minimum lethal concentration for 3 minutes was derived are tabulated herewith.

Dog Number	Collapse in seconds	Concentration	Result	
1432	125	0.26	Recovered	)
1430	95	0.306	Recovered	) 0/4*
1439	170	0.312	Recovered	) Av.conc.
1428**	90	0.33	Recovered	) 0.302
1437	85	0.33	Died 42 hours	)
1431	75	0.34	Recovered	) 3/5*
1441	85	0.34	Recovered	) Av.conc.
1438	120	0.34	Died 4 days	) 0.34
1435		0.35	Died 46 hours	)
1434	95	0.355	Recovered	)
1427	85	0.36	Died at exposure	) 4/5*
1371	95	0.36	Died 84 hours	) Av.conc.
1429	87	0.37	Died 12 hours	) 0.376
1385	55	0.439	Died 16 hours	)
1370	70	0.47	Died 60 hours	)
1383		0.487	Recovered	) 4/5*
1384	60	0.493	Died at exposure	) Av.conc.
1386	60	0.493	Died 12 hours	) 0.487
1382	68	0.493	Died at exposure	)
1381	72	0.493	Died 8 days	)
1388	60	0.499	Died at exposure	) 5/5*
1387	85	0.506	Died 36 hours	) Av.conc.
1373	60	0.52	Died at exposure	) 0.507
1372	75	0.52	Died at exposure	

* The numerator indicates the number of deaths and denominator shows number of dogs used.

**This dog died after 20 days, during which time his hind legs were paralyzed. Because of the unusually long period elapsing between gassing and death he is classed as a recovery.

The minimal lethal concentration for 180 seconds is placed at 0.34 milligrams per liter.

7½ MINUTE EXPOSURE.

The data from which the minimum lethal concentration for 7½ minutes was derived are tabulated herewith:

Dog Number	Collapse in seconds	Concentration	Result	
1359	450	0.154	Recovered	)1/2*
1366	150	0.19	Died 5 days	)Av.conc.
				)0.172
1368	145	0.206	Died at exposure	)
1369	135	0.202	Recovered	)3/5*
1367	140	0.212	Died at exposure	)Av.conc.
1364	140	0.212	Died at exposure	)0.208
1365	225	0.21	Recovered	)
1358	180	0.22	Died 4½ days	)
1362	130	0.24	Died 36 hours	)5/5*
1361	75	0.25	Died at exposure	)Av.conc.
1357	95	0.268	Died at exposure	)0.251
1363	120	0.28	Died at exposure	)

*The numerator indicates the number of deaths and denominator shows number of dogs used.

The minimal lethal concentration for 450 seconds is placed at 0.208 milligrams per liter.

MONKEYS

30 SECOND EXPOSURE

Concentration	Collapse in seconds	Result	
1.43	35	Recovered	
1.94	43	Died	

The lethal concentration for monkeys lies between 1.43 and 1.94 milligrams per liter for 30 seconds.

60 SECOND EXPOSURE

0.723	50	Recovered	
0.824	45	Died	

The lethal concentration for monkeys lies between 0.723 and 0.824 milligrams per liter for 60 seconds.

3 MINUTE EXPOSURE

0.506	80	Recovered.	Mice 4/5; Guinea pig recovered; Dog died; Rabbit died.
0.663	65	Died 4 days	
0.79	80	Died	

The lethal concentration for monkeys lies between 0.506 and 0.663 milligrams per liter for 180 seconds.

7½ MINUTE EXPOSURE

0.26	190	Recovered.	Guinea pig recovered; Rabbit died.
0.268	100	Recovered.	Dog died.
0.326	120	Died.	

The lethal concentration for monkeys lies between 0.268 and 0.326 milligrams per liter for 450 seconds.

MICE

10 SECOND EXPOSURE

Concentration	Result
2.35	3/5

30 SECOND EXPOSURE

0.488	0/5	
0.660	2/5	8/15
0.805	3/5	Av.conc.
0.845	3/5	0.77
1.73	5/5	

The minimal lethal concentration for 30 seconds on mice is placed at 0.77 milligrams per liter.

60 SECOND EXPOSURE

0.422	0/5	3/20	
0.488	0/5	Av.conc.	
0.503	2/5	0.482	
0.515	1/5		
0.541	1/5	9/15	
0.576	5/5	Av.conc.	
0.584	3/5	0.567	
0.673	5/5	15/15	
0.857	5/5	Av.conc.	Gassed with rabbit and dog #1389. Both died at exposure.
0.858	5/5	0.796	Guinea pig recovered.

The minimal lethal concentration for 60 seconds on mice is placed at 0.567 milligrams per liter.

3 MINUTE EXPOSURE

0.277	0/5		
0.337	2/5)	10/15	
0.373	3/5)	Av.conc.	
0.393	5/5)	0.367	Gassed with rabbit. Recovered.
0.436	4/5)	8/10	
0.506	4/5)	Av.conc.	
		0.471	Gassed with monkey and guinea pig. Recovered. Dog and rabbit died at exposure.

The minimal lethal concentration for 3 minutes on mice is placed at 0.367 milligrams per liter.

7½ MINUTE EXPOSURE

0.177	0/5)	0/20	
0.181	0/5)	Av.conc.	
0.1927	0/5)	0.193	
0.222	0/5)		
0.24	2/5)	8/15	
0.241	2/5)	Av.conc.	
0.246	4/5)	0.242	
0.28	4/5)	9/10	Gassed with guinea pig and dog. Former recovered, dog died.
0.338	5/5)	Av.conc.	
		0.309	

The minimal lethal concentration for 7½ minutes on mice is placed at 0.242 milligrams per liter.

10 MINUTE EXPOSURE

0.08	0/5)	0/10
0.163	0/5)	Av.conc. 0.121
0.177	2/5)	11/15
0.1953	5/5)	Av.conc.
0.199	4/5)	0.190
0.203	1/5)	8/15
0.208	3/5)	Av.conc.
0.24	4/5)	0.217
0.248	5/5)	9/10
0.256	4/5)	Av. conc. 0.252

The minimal lethal concentration for 10 minutes on mice is placed at 0.190 milligrams per liter.

GUINEA PIGS

30 SECOND EXPOSURE

Concentration	Collapse in seconds	Result
1.85	60	Recovered
2.05	45	Recovered
2.11	50	Recovered
2.21	50	Recovered
2.35	45	Recovered
2.71	30	Died
3.04	30	Died

The lethal concentration for 30 second exposure on guinea pigs lies between 2.35 and 2.71 milligrams per liter.

60 SECOND EXPOSURE

0.857	55	Recovered. Dog #1389 died. Mice 5/5. Rabbit died.
1.2	45	Recovered
1.5	40	Recovered
1.78	47	Died

The lethal concentration for 60 second exposure on guinea pigs lies between 1.5 and 1.78 milligrams per liter.

3 MINUTE EXPOSURE

0.506	not affected	Recovered. Gassed with dog 1387. Died. Rabbit died.
0.75	75	Recovered
0.80	85	Recovered
0.812	70	Died
1.2	55	Died

The lethal concentration for 3 minute exposure on guinea pigs is placed at 0.812 milligrams per liter.

7½ MINUTE EXPOSURE

0.26	285	Recovered. Monkey recovered. Rabbit died.
0.28	not affected	Recovered. Dog 1363 died. Mice 4/5.
0.322	360	Recovered. Rabbit died.
0.38	not affected	Recovered.
0.361	210	Died
0.373	270	Died

The lethal concentration for 7½ minute exposure on guinea pigs lies between .322 and .38 milligrams per liter.

RABBITS

30 SECOND EXPOSURE

Concentration	Collapse in seconds	Result
1.24		Recovered
1.72	65	Died 48 hours
2.35	57	Died
2.71	60	Died
3.04	55	Died

The lethal concentration for 30 seconds on rabbits lies between 1.24 and 1.72 milligrams per liter.

60 SECOND EXPOSURE

0.59		Recovered
0.706	Did not fall	Recovered
0.713	" " "	Recovered
0.857	50	Died. Mice 5/5. Guinea pig recovered. Dog 1389 died.

The lethal concentration for 60 seconds on rabbits lies between 0.713 and 0.857 milligrams per liter.

3 MINUTE EXPOSURE

0.393	Not affected	Recovered. Mice 5/5
0.409	" "	Recovered
0.422	" "	Recovered
0.506	95	Died. Mice 4/5. Monkey recovered. Dog 1387 died. Guinea pig recovere.
0.554	105	Died

The lethal concentration for 3 minutes on rabbits lies between 0.422 and 0.506 milligrams per liter.

7½ MINUTE EXPOSURE

0.24	240	Recovered. Dog 1362 died.
0.26	285	Died. Monkey recovered. Guinea pig recovered.
0.32	300	Died. Guinea pig recovered.

The lethal concentration for 7½ minutes on rabbits lies between 0.24 and 0.26 milligrams per liter.

COMPARATIVE DATA OF ANIMALS GASSED TOGETHER.

30 SECOND EXPOSURE

Animal	Concentration	Collapse in seconds	Result
Rabbit	2.71	60	D*
Guinea pig	2.71	30	D
Rabbit	2.35	57	D
Guinea pig	2.35	45	Recovered
Rabbit	3.04	35	D
Guinea pig	3.04	30	D
Rabbit	1.72	35	Died 48 hours
Mice	1.72	35	5/5

1 MINUTE EXPOSURE

Rabbit	0.857	50	D
Mice	0.857		5/5
Guinea pig	0.857	55	Recovered
Dog 1369	0.857	30	D
Monkey	0.824	45	D
Dog 1390	0.824	50	D
Canary	0.844	10	D
Dog 1394	0.844	50	D

3 MINUTE EXPOSURE

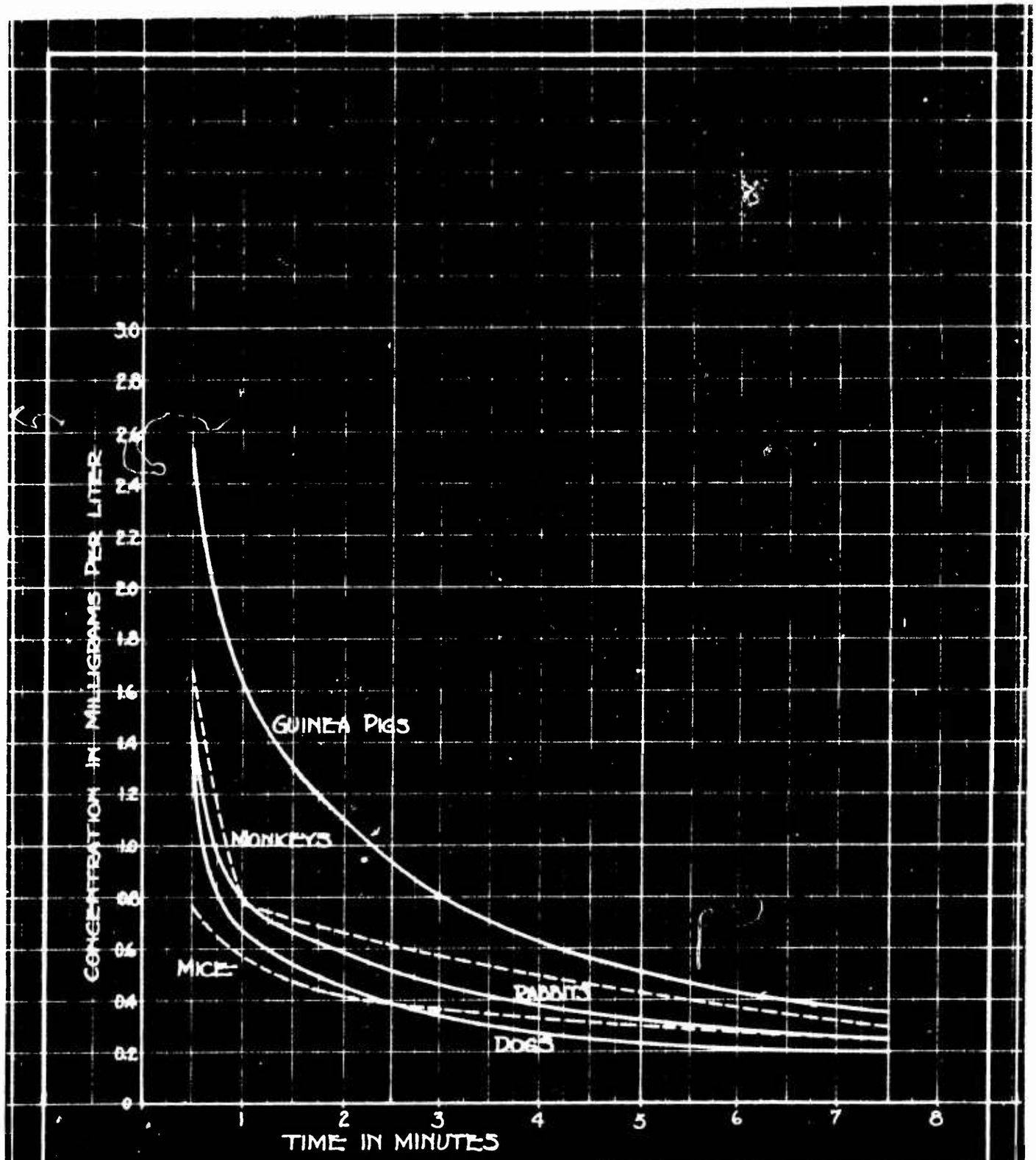
Rabbit	0.393	60	Recovered
Mice	0.393		5/5
Dog 1387	0.506	75	Died in 36 hours
Guinea pig	0.506	not affected	Recovered
Rabbit	0.506	45	D
Mice	0.506	50	4/5
Monkey	0.506	80	Recovered

*D indicates death within 10 minutes after exposure.

COMPARATIVE DATA OF ANIMALS GASSED TOGETHER

7½ MINUTE EXPOSURE

Animal	Concentration	Collapse in seconds	Result
Rabbit	0.24	240	Recovered
Dog 1362	0.24	130	Died in 36 hours
Monkey	0.26	190	Recovered
Guinea pig	0.26	300	Recovered
Rabbit	0.26	265	D
Monkey	0.268	100	Recovered
Dog 1357	0.268	95	D
Mice	0.28	60	4/5
Guinea pig	0.28	not affected	Recovered
Dog 1363	0.28	120	D
Guinea pig	0.32	390	Recovered
Rabbit	0.32	300	D



THE TOXICITY OF HYDROCYANIC ACID GAS

LETHAL CONCENTRATIONS OF HCN FOR VARIOUS ANIMALS —		
REPORT NO. EAMRD 20		
12-4-23		EAE-3-1040

VI. SYMPTOMATOLOGY AND PATHOLOGY OF HYDROCYANIC ACID GASSING.

A. Symptomatology. Sollmann summarizes the symptoms in man as follows, "In the so-called apoplectic form; i.e., when very large doses are taken, the patient may fall unconscious, often with a loud cry, within ten seconds, and die within two to five minutes, after some convulsions. Ordinarily, the course is rather more prolonged; several minutes may elapse after taking the poison before any effect is noticed; death occurs between fifteen minutes to an hour.

The symptoms consist in vertigo, mental dimness, headache, palpitation; then dyspnea, which may be very great from stimulation of the respiratory center; the patient then becomes totally unconscious and falls into violent convulsions. During this stage the heart may be greatly quickened. The respiration becomes first difficult and then ceases. The heart at this time is very much weakened, but still continues to beat for a short time and then stops.

The mortality is very high: 95 per cent. If the patient survives an hour, recovery is the rule. It is often followed by persistent headache, tremors, etc."

In the dogs gassed by us the symptoms were as follows: Symptoms during exposure: The dogs noticed the gas in a few seconds, sniffing and showing only a very slight degree of excitement. Weakness and unsteadiness ensued, followed by a sudden collapse, the animal falling heavily and crying or howling with clenched jaws and retracted lips. This was rapidly followed by a spastic paralysis, first of the hind quarters and then of the whole body, the animal assuming the position of opisthotonos. General convulsions were noted in many dogs. Involuntary evacuations of urine and faeces were the rule. The mucous membranes were a bright pink. The respirations ceased early depending on the concentration and length of exposure. Prior to ceasing it was usually of a Cheyne-Stokes type, the dogs taking an occasional gasping respiration. In some of the animals no respiration was noted after the initial stop. Salivation and vomiting occurred in a few cases, especially in dogs lightly gassed.

The heart beat was slow and feeble. The relation of collapse to length of exposure and concentration is shown in the toxicity tables.

Symptoms following exposure:

1. Dogs dying within an hour. These animals lay in a stupor on the floor. A few minutes after removal from the cage a gasping inspiration would be made, followed by a long pause. Respiration of the Cheyne-Stokes type would then be established which would become weaker and weaker the respirations finally ceasing. The heart continued to beat for some minutes after respiration had ceased.

2. Dogs recovering immediately. These animals showed the typical "reverse poisoning" of cyanide action. After the first inspiration they would pass through the stages of Cheyne-Stokes respiration, followed by rapid breathing and a return to the normal. The stupor of unconsciousness was followed by mild convulsions and twitchings of the limbs; succeeded by a recovery of power in the fore-quarters, the animal dragging itself around by the front legs. Recovery would then be rapid, the animal next passing through the stage of unsteadiness and weakness. Vomiting often occurred at this point. In two or three hours such dogs appeared normal except for slight weakness and a watery discharge from the eyes.

3. Late Deaths. All of the classical descriptions of cyanide poisoning in cases not immediately fatal, refer to the "immediate recovery", and state that no delayed effects or deaths occurred.

In our series we found that there was an upper limit of low concentrations where all animals promptly recovered and a lower limit of high concentrations in which all animals promptly died. However between these two limits was an intermediate zone of concentrations, in which an animal might die at once, might recover completely, or might live for several days only to die finally. These latter dogs presented a picture that, so far as we know, has never before been described. The animals lay prostrate in the cages, breathing slowly, but usually showing no other signs of life. They were apparently conscious and in certain instances whined and cried, but were unable to move. They were totally unable to eat or drink even when water was held in front of them. In certain instances a continuous swimming or clawing motion was made with the forelegs probably caused by irritation of the nerve centers. These animals undoubtedly suffered from a permanent injury to the nerve centers probably of the lower brain and cord.

This injury may have been due to the specific action of the cyanide, though this is improbable because if cyanide caused a specific permanent injury the prompt recoveries so characteristic of cyanide poisoning could hardly occur at all. The injury to the nerve centers is more probably caused by the prolonged deprivation of oxygen. Similar effects follow carbon monoxide poisoning, and as Haldane says, "Anoxaemia not only stops the machinery, but wrecks the machine". It is probable that the nerve centers suffered true degenerative changes during their deprivation of oxygen though we have been unable to demonstrate such changes by ordinary pathological methods.

B. Pathology. Twenty-two of the dogs dying after exposure to hydrocyanic acid gas were studied with regard to the pathological lesions produced. In this report the dogs are grouped according to the time of death in relation to the exposure: Group I includes those dying at the time of exposure, and Group II those which survived the gassing but died subsequently at intervals varying from 6 hours to 20 days. Findings are reported regardless of concentration and length of exposure.

Group I: Dogs dying as an immediate result of the exposure.

There are three dogs in this group. Externally no changes could be seen. Internally the most noticeable gross finding was an excessive pericardial effusion which in one case was blood tinged. On the heart of one dog there were a number of petechial hemorrhagic areas extending but a short distance into the muscle. The majority of these areas were along the auriculo-ventricular sulcus. A larger one was also found at the apex. When the respiratory system was examined the mucosa of the larynx and trachea was found to be normal. In one case the lumen of the trachea was filled with froth. The lungs of this dog were bright pink in color and heavier and firmer than normal. Microscopic examination revealed an extensive pulmonary edema, which in places hid the lung framework. There was also a marked congestion and considerable hemorrhage. Many blood vessels were surrounded by wide rings of edematous tissues and many bronchi were filled with edema fluid. The mucosa of one large bronchus appeared swollen.

Of the lungs of the other two dogs of this group one pair grossly appeared normal while the other was bright pink in color and slightly heavier and less elastic than normal. Microscopically the former showed a very little scattered atelectasis only, while the

latter showed irregularly distended alveoli in some of which were found hemorrhage and edema fluid. The capillaries of the alveolar walls were injected and all blood vessels were filled with blood. There was also some patchy atelectasis.

Group II: Dogs dying from 6 hours to 20 days after exposure.

This group includes nineteen dogs. The earliest deaths were at 6 hours and the latest 12 days after exposure. The dogs which survived the longer period were poorly nourished. Otherwise no unusual external changes were noted. Nine dogs in this group showed marked pericardial effusions and in one dog ascites was noted. In 3 dogs unclotted blood almost black in color was found in the heart; in two there was a slight dilatation of the right ventricle. These conditions were found in deaths after 30 hours. Prior to this time the heart appeared normal. In the earliest deaths no changes were found in the mucosa of the larynx and trachea. Of the two dogs which died at 6 hours one had lungs which grossly appeared normal and microscopically showed only small areas of partial atelectasis. The other dog had lungs which were bright pink in color, heavier and more voluminous than normal and microscopic examination showed some congestion, hemorrhage, a little edema, and numerous small scattered areas of partial atelectasis. In some of the small bronchi there was an exudate consisting of desquamated epithelial cells mixed with mucus. In dogs dying at 12 hours or later the lungs were congested and edematous grossly. Microscopically these findings were confirmed and in addition perivascular edema, some little hemorrhage in the alveoli, atelectasis, and acute emphysema were noted. Three cases of broncho pneumonia were found in dogs dying after 24 hours. Microscopic study showed purulent bronchitis associated in these pneumonias. There was one case of bronchiolitis and two cases in which a fairly extensive hemorrhage was found in the large bronchi. Congestion, hemorrhage, some edema, scattered atelectasis, and acute emphysema were regularly found in deaths after 24 hours. In one case there was a peribronchitis involving bronchi of all sizes and in twenty-five per cent of the cases in the bronchi, especially the small ones, there was an exudate composed of desquamated alveolar epithelial cells, cellular debris, mucus and sometimes a little fibrin.

The largest percentage of dogs in both groups showed congestion of the liver and of the kidneys both grossly and microscopically and a normal condition of the other abdominal organs.

Sections were taken from the motor areas, from the medulla, and at varying levels through the spinal cords of a number of dogs dying at varying intervals after exposure. The hematoxylin-eosin stained preparations of these areas showed nothing noteworthy. The gross examination of the brain and cords of these dogs had shown a slight engorgement of the sinuses.

SUMMARY OF FINDINGS

A. Dogs dying acutely. (Three dogs.)

1. Pericardial effusion was found in one dog.

2. The punctiform hemorrhages referred to in the literature on cyanide poisoning were found in only one of three cases.

3. Grossly the lungs showed an abnormally bright pink color.

4. It is well known that there are few marked pathological changes after sudden death from hydrocyanic acid. The marked pulmonary edema found in one of these dogs was evidently adventitious, and we are quite at a loss to explain why it should have occurred.

B. Dogs dying from 6 hours to 20 days.

1. Pericardial effusion was found in 50% of the dogs autopsied. In all animals autopsied after exposure to other gases pericardial effusion has been almost unknown.

2. Histologically the findings of note in the lungs were as follows in the order of their importance (based on the severity of the lesion and the constancy of its appearance): (a) congestion, (b) edema, and (c) the presence in the small bronchi of an exudate of cellular debris, mixed with mucus and fibrin.

3. The pulmonary changes in these dogs may be explained partly as hypostatic congestion occurring in paralyzed animals. But it is also probable that hydrocyanic acid produces a specific congestion of the lungs in any animals that live long enough to develop it. Hydrocyanic acid is a general protoplasmic poison and it is quite possible that it thus causes the death of many cells in the bronchi and alveoli which must have been saturated with the poison. Naturally these necrotic cells would be sloughed off in animals surviving the exposure for several days, and the irritation would be followed by a certain degree of congestion and even some pulmonary edema.

INDEX OF EDEMA

A study was made to determine the relation between the weight of the lungs and that of the empty heart in order to get an idea as to the fluid or cellular content of the lungs. The normal ratio is approximately 1:1.5. In this series of dogs the average ratio for Group I is 1:1.63, for Group II 1:1.82. The increase over the average as found in Group II was due in all probability to the congestion and pneumonia present in the lungs of the dogs of this group.

GROUP I

Dog Number	Weight of lungs	Weight of heart	Index of edema
1456	133	70	1.90
1455	147	75	1.96
1454	125	120	1.04
		Av.	1.63

GROUP II

1450	45	30	1.50
1449	140	74	1.89
1412	173	72	2.40
1387	85	37	2.30
1362	270	90	3.00
1437	132	96	1.37
1417	255	115	2.13
1435	228	116	1.90
1448	32	22	1.45
1446	54	32	1.70
1438	--	--	----
1392 A	152	80	1.90
1433	--	--	----
1375 A	110	61	1.8
1359 A	91	43	2.1
1358	190	92	2.00
1366	250	170	1.47
1424	155	93	1.55
1381	50	39	1.28
1428	130	102	1.27
		Av.	1.82

TABLE OF DEATHS.

Dog Number	Time of Death after exposure.
1456	Immediately
1455	"
1454	2 Minutes
1450	6 Hours
1449	6 "
1412	12 "
1387	30 "
1362	36 "
1437	42 "
1435	48 "
1417	60 "
1448	3 Days
1446	3 "
1359	4 "
1375	4 "
1392	4 "
1433	4 "
1358	5 "
1366	5 "
1381	8 "
1424	8 "
1426	20 "

VII. Discussion of American, British and German Toxicity Figures.

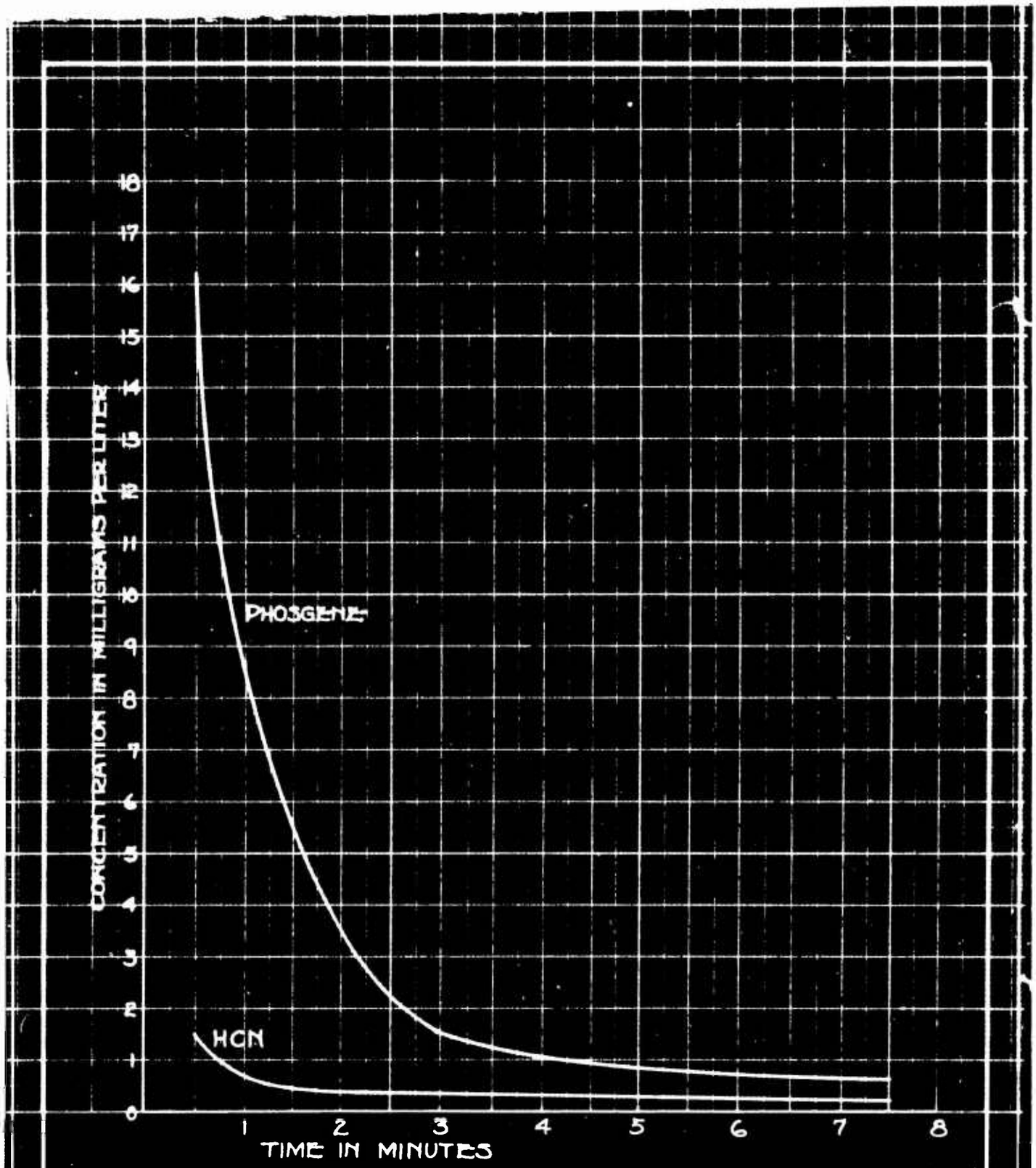
A. Owing to differences in methods, length of exposure and variations in numbers and kinds of animals used a direct comparison of our figures with the British and German figures is difficult. An examination of the following table shows however that our figures are consistently lower than the British. This is probably due to the fact that our gassing chamber provides instantaneous exposure.

Lethal points

English	Edgewood Arsenal
Monkeys	
3 min. 1.2 mg/l = 1/2	Between 0.506 and 0.663 mg/l
6 min. 0.6 " = 0/2	7½ min. Between 0.268 and 0.326 mg/l.
Dogs	
30 sec. 1.2 mg/l = 0/2	1.49
1 min. 0.60 " = 2/2	0.67
3 min. 0.40 " = 2/2	0.34
10 min. 0.24 " = 2/3	7½ min. 0.208
Rabbits	
1 min. 1.2 mg/l = 2/2	between 1.24 and 1.72 mg/l
3 min. 0.60 " = 3/4	" 0.422 " 0.506 "
7 min. 0.48 " = 1/2	7½ min. " 0.24 " 0.26 "

B. The experiment to which Professor Barcroft submitted himself, and in which he successfully withstood a concentration of 1-2000 (0.603 mg/l) can be questioned on the following grounds:

1. It is not stated whether the dog died or not.
2. Our results show a wide variation in the individual resistance of dogs. The one dog used in this experiment may have been a susceptible animal.
3. A concentration a few hundredths of a milligram higher, or an exposure of a few more seconds might have sufficed to render Professor Barcroft a casualty as he already felt slight nausea and inability to concentrate.



THE TOXICITY OF
HYDROCYANIC ACID GAS

COMPARISON OF LETHAL CONCENTRATIONS
FOR PHOSGENE AND HCN ON DOGS.

REPORT NO. EAMRD 20

12-4-23 | EAE-S-1041

4. The German figures show that the toxicity figures for various animals such as the monkey, dog and cat are very close to each other. The British, basing their view on the experiments detailed above, state that there is a wide divergence in the toxicity of hydrocyanic acid gas for different species. Our work shows that while this is true to a limited degree on short exposures, the graphs for different species approach each other and in some cases after longer exposure, actually merge. Even at short exposures the most resistant animal, the guinea pig, was only slightly more resistant than the general group.

C. That there is permanently ineffective concentration of hydrocyanic acid is probably true, lying around 0.03 mg/l. But long exposures to even smaller concentrations would undoubtedly produce the symptoms noted in factory workers of dizziness and frontal headache.

D. A review of our figures shows that the time of collapse varies greatly and in many cases bears no direct relationship to the fatal or non-fatal outcome of the gassing. A concentration of 2.0 mg/l always caused dogs to collapse in less than 35 seconds. Flury found that a concentration of 1.0 mg/l caused collapse in cats in from 40 to 70 seconds. It is of interest to note in our 30 second series that all of the dogs except two collapsed after the gas was removed. In this connection it could easily occur that a man after breathing a high concentration might die after masking.

E. The table of "Animals gassed together" confirms the graphs of relative susceptibility of species both in time of collapse and in after results.

VIII. Comparison with Phosgene.

By consulting the curves submitted it will be seen that hydrocyanic acid is about ten times as effective as phosgene for 30 second exposures. But it must be borne in mind that hydrocyanic acid produces but few if any symptoms until a lethal concentration is reached, whereas phosgene possesses the power of producing casualties at concentrations considerably below lethal.

In order to make a comparison of the lethal concentration of hydrocyanic acid for short exposures with phosgene the following experiment was made. Three dogs were exposed in the same gassing chamber to a concentration of 4.3 mg/l for 30 seconds. They were then removed, their symptoms noted and haemoglobin determinations made to determine the degree of pulmonary edema caused. The results, tabulated below show that a concentration of 4.3 mg/l killed one dog and the marked decrease in haemoglobin immediately following gassing indicates injury to the lungs of the others.

EXPOSURE 30 SECONDS. CONCENTRATION 4.3. TIME OF GASSING 8.17 A.M. 11-16-23.

HAEMOGLOBIN

Dog 1432 A.	11-15-23	Normal	81	per	cent	
	11-16-23	8.50 A.M.	73	"	"	This dog vomited at 8.39 A.M. Became restless with labored respiration at 12 M. when gums were blue and cyanotic. It died of pulmonary edema during the night.
		10.15 A.M.	72	"	"	
		11.20 A.M.	71	"	"	
		1.30 P.M.	84	"	"	
		2.30 P.M.	84	"	"	
		3.30 P.M.	82	"	"	
		4.40 P.M.	84	"	"	
Dog 1413 A.	11-15-23	Normal	61	per	cent	
	11-16-23	8.40 A.M.	48	"	"	This dog fell down in the chamber 15 seconds after phosgene was turned on. No further symptoms occurred and next day the dog was apparently normal. The dog lived.
		10.00 A.M.	50	"	"	
		11.10 A.M.	49	"	"	
		1.25 P.M.	50	"	"	
		2.25 P.M.	50	"	"	
		3.25 P.M.	49	"	"	
		4.30 P.M.	50	"	"	
	11-17-23	9.30 A.M.	54	"	"	
Dog 1416 A.	11-15-23	Normal	72	per	cent	
	11-16-23	8.45 A.M.	59	"	"	This dog was restless at first when removed from the chamber, but thereafter appeared normal. The dog lived.
		10.05 A.M.	60	"	"	
		11.15 A.M.	60	"	"	
		1.25 P.M.	58	"	"	
		2.25 P.M.	57	"	"	
		3.25 P.M.	61	"	"	
		4.35 P.M.	62	"	"	
	11-17-23	9.35 A.M.	64	"	"	

Three more dogs were exposed to a concentration of 3.93 mg/l of phosgene for 30 seconds. These three dogs showed a slight rise of temperature following gassing, an increase in pulse rate and respiratory rate. Twenty-four hours later they appeared normal, and were killed by injection of magnesium sulphate in the heart. At post mortem, the first dog showed marked pulmonary edema scattered through all lobes of the lungs, the heart lung ratio 1 to 3.1 or nearly twice the normal. The second dog showed one small area of congestion and edema in the right middle lobe, the heart lung ratio being 1 to 1.32 or about normal. The third dog was normal.

These dogs were very active before gassing and very quiet afterwards. It is impossible to say just what degree of injury will make casualties of men, because individuals differ so remarkably in courage, will power and desire to carry on. However it is believed that should any number of men be affected to the extent that these dogs were, a certain percentage of casualties would be produced. From the tactical point of view, a casualty is of more advantage than a death. The casualty is out of action and in addition requires several men to care for him.

On the other hand is the undoubted moral effect produced on the enemy by the terror and uncertainty produced by a lethal gas of the properties of hydrocyanic acid. It would not be necessary to use this gas often in order to produce this moral effect, for the enemy could never be certain when the next attack would come. It is also possible that hydrocyanic acid would produce deaths even after the mask was applied if a sufficient concentration was inhaled prior to masking. At 30 second exposures the majority of the dogs died after the gas was shut off. On the other hand a concentration of 4.mg/l. of phosgene would undoubtedly be quite irritating and men would mask promptly, so that casualties might not occur. For these reasons it appears that there is a real place for hydrocyanic acid in the list of chemical warfare agents, provided its physical peculiarities permit of its use. With this aspect of the case this report cannot deal.

Submitted by:

G. C. Armstrong

A. R. Koontz

M.G.Witherspoon

Supervised by:

D.C.Walton,
Lieut. Comdr., M.C.,U.S.N.
Chief, Department of Toxicology.

Approved by:

Edward B. Vedder,
Lt.Col.,M.C., U.S.A.
Chief, Medical Research Division.

The Toxicity of Hydrocyanic Acid Gas on Dogs, Monkeys, Mice, Guinea Pigs and Rabbits.

Work begun: September 20, 1923.
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DEPARTMENT OF THE ARMY
US ARMY RESEARCH, DEVELOPMENT AND ENGINEERING COMMAND
EDGEWOOD CHEMICAL BIOLOGICAL CENTER
5183 BLACKHAWK ROAD
ABERDEEN PROVING GROUND, MD 21010-5424

REPLY TO
ATTENTION OF

FEB 27 2015

RDCB-DPS-RS

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, Virginia 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:

a. C.J. West, Cyanogen Chloride, from Chemical Warfare Monographs Volume 50, Pharmacological Data Part I. War Department CWS, Research Division, American University Experiment Station, Washington, DC, April 1919 (Dist. E).

b. C.J. West, Cyanogen Chloride, from Chemical Warfare Monographs Volume 50, Pharmacological Data Part II. War Department CWS, Research Division, American University Experiment Station, Washington, DC, June 1919 (Dist. E).

c. G.C. Armstrong, A.R. Koontz and M.G. Witherspoon, The Toxicity of Hydrocyanic Acid Gas on Dogs, Monkeys, Mice, Guinea Pigs and Rabbits. EAMRD-20. War Department, CWS, Edgewood Arsenal, MD, 31 December 1923 (Dist. E).

d. A.M. Ginzler, The Pathology of CK by Inhalation, Technical Corps Technical Command, Army Chemical Center, MD, CBRNIAC-CB-176432, 19 Jun 45 (Dist E).

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 Ms. Adana Eilo, ECBC Security Specialist, (410) 436-2063 or adana.l.eilo.civ@mail.mil.

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