

STUDY OF THE TOXICITY OF LEAD T. TRA. HIND.

by

W. A. Eldridge

October 5, 1924.

A STUDY OF THE TOXICITY OF LEAD TETRA ETHYL

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I. INTRODUCTION.

The object of the following tests was to determine the toxicity of Lead Tetra Ethyl upon animals and to study the symptoms produced by this compound. Four different methods were used to administer the compound and lethal points were established by each method. The methods employed were as follows: Local application, subcutaneous injection, intravenous injection, and inhalation.

II. SUMMARY:

1. The lethal point by skin application was placed at 0.6 cc. or 0.996 gram per kilo for guinea pigs and at 0.3 cc. or 0.498 gram per kilo for dogs. 1 cc. of pure Lead Tetra Ethyl weighs 1.659 grams.
2. The lethal point for guinea pigs by subcutaneous injection is approximately 0.06 cc. or 0.132 gram per kilo.
3. The lethal point for dogs by intravenous injection is placed at 0.011 cc. or 0.018 gram per kilo.
4. The lethal concentration for mice by inhalation is placed at 5.11 milligrams per liter.
5. The evidence indicates that smaller doses are cumulative in action by whatever route administered.
6. When an animal receives a lethal dose by skin application, its life may be saved by washing with kerosene followed by tincture green soap and water, provided this treatment is carried out within thirty minutes after application.

III. HISTORICAL.

Although chronic lead poisoning is the commonest of all forms of metallic poisoning, true acute lead poisoning, that is the effect of a sudden absorption of lead in man has been hitherto unknown. When a large quantity of some soluble salt of lead is swallowed, it gives rise to the ordinary symptoms of irritant poisoning: namely, nausea, vomiting, pain in the abdomen, violent purging, weakness and collapse.

In animals also, it has been difficult hitherto to produce acute lead poisoning because when most forms of lead are injected the proteins of the blood are precipitated and death so produced is purely mechanical, and only local symptoms were produced by administration by mouth. However Harnack injected salts of lead triethyl. In the frog this produced general paralysis apparently by the action of lead on the central nervous system. In the dog the symptoms following intravenous injection were weakness and paralysis, violent diarrhoea and colic, chorea-like movements, tremors, and convulsions. The diarrhoea was found to be due to violent contractions of the intestinal walls, which maintained a degree of contraction even when no peristaltic wave was passing. (Cushny - Pharmacology and Therapeutics, page 663.)

Lead tetra ethyl was developed by the General Motors and Du Pont corporations as an addition to motor fuels. But soon after large scale production was commenced, a number of men handling this product became ill and several of them died. The following description of the symptoms was included in a report to the Standard Oil Company by Drs. Thompson and Schoenleber, rendered May 18, 1924.

"The first symptoms observed are a marked fall in blood pressure sometimes as low as sixty points below normal. There is an accompanying fall in body temperature which has been recorded as low as 94.6 degrees Fahrenheit or four degrees below normal. The heart action is slowed, the pulse having dropped in one case as low as 48, that is, twelve or more counts below normal. There is at first some digestive disturbance, such as loss of appetite, vomiting and a tendency to looseness of the bowels. Vertigo may be present. The red blood corpuscles show marked changes in size and shape. The blood in one of the fatal cases failed entirely to

coagulate and at autopsy showed an unusual color such as is observed in carbon monoxide poisoning. There is no cyanosis and no shortness of breath, nor is headache or other pain complained of. The urine remains normal usually but in one case reported treated by Dr. Art of Harvard lead was present in it. Following these symptoms in severe cases other phenomena appear indicative of profound cerebral disturbance. The victim suffers from persistent insomnia and becomes delusional, extraordinarily restless and talkative. His gait is staggering like that of a drunken man, but there is no paralysis and convulsions do not appear. There is exaggerated movement of all the muscles of the body accompanied by perspiration and the patient finally becomes violently maniacal, shouting loudly, leaping out of bed, attempting to smash furniture or windows and behaving like a violent case of delirium tremens. Morphine only accentuates the symptoms. The victim may finally die in exhaustion. One man smashed a window and cut his hand badly. He had delusions of vision, seeing imaginary groups of persons, and accusing the Doctor of trying to cut him up. Another man saw the wall paper converted into swarms of moving flies and thought pictures of his family on the walls were alive and moving about.

Of the two fatal cases the body temperature in one patient rose to 110 degrees just before death. Both these men had been at work only five weeks. The elder, 53 years of age, was not very vigorous, originally having a chronic fibroid condition of the lungs. The younger man was of fine physique. Dr. McGinn, who has had a very extensive general practice, stated that he never in his life had seen anyone die in such agony as these two men as he said "they died yelling". One man had to be strapped in bed by an expert accustomed to restraining the insane.

As in nearly all poisonings of industrial origin considerable personal idiosyncrasy may exist as to bodily resistance. Many of the workmen showing only slight symptoms have continued at work. In other cases quite marked symptoms have developed within from three to six hours. In one case the blood pressure dropped in only three and a half hours after beginning work - from 190 to 112 - a fall commensurate with that which occurs in excessive hemorrhage. Convalescence from the severe symptoms is quite protracted and may occupy from six to ten weeks."

The following table which was furnished us by the chief surgeon of the Du Pont Company,* records the symptoms observed in twenty-eight such cases.

SYMPTOMS RECORDED IN TWENTY-EIGHT CASES
OF TERMINAL LEAD POISONING.

(The figures refer to the number of cases in which each symptom was observed)

Insomnia	23
Anorexia	18
Nausea	18
Morning vomiting.....	10
Abdominal cramps	12
Unaccustomed and annoying dreams.....	11
Bodily weakness	16
Decided loss of weight	9
Markedly diminished blood pressure	20
Slowing of pulse rate	7
Photophobia	1
Metallic taste in the mouth	6
Lead line on the gums	4
Subnormal temperature	19
Hyper-acidity of the urine	18
Albumin in the urine	2
Acetone in the urine	1
Skin test for lead	12
Tremors	6
Ectoma	3
Increased muscular reactions	7
Dilated pupils	1
Itching of the skin	4
Marked drowsiness in the daytime	1
Sluggish pupils	2
Headache	7
Vertigo	10
Irritation of mucous membranes of the nose and throat...	1

* Supplied by Robert M. Kelso and based on observations made in Dayton, Ohio

The physicians employed by these companies were of the opinion that the toxicity of lead tetra ethyl was caused partly by the compound as a whole and could not be ascribed entirely to lead poisoning, especially in view of such symptoms as insomnia and mental excitement. But in view of the fact that little has been known heretofore concerning acute lead poisoning, and since all the symptoms described have been previously described as occurring in cases of chronic lead poisoning, we are inclined to the opinion that the toxic effects of lead tetra ethyl are simply a manifestation of acute lead poisoning. Thus Osler, (Principles and Practice of Medicine, Ninth Edition, page 394) says,

"SYMPTOMS--ACUTE FORM.--We do not refer here to the accidental or suicidal cases, which present vomiting, pain in the abdomen, and collapse symptoms. In workers in lead there are several manifestations which follow a short time after exposure and set in acutely. There may be, in the first place, a rapidly developing anaemia. Acute neuritis has been described, and convulsions, epilepsy, and a delirium, which may be not unlike that produced by alcohol. There are cases in which the gastro-intestinal symptoms are intense and rapidly prove fatal. These acute forms occur more frequently in persons recently exposed, and more often in winter than in summer. Da Costa reported the onset of hemiplegia after three days' exposure to lead."

"Certain of the cases with colic may present the features of an acute intra-abdominal inflammatory condition. A case may be admitted to the surgical wards with a diagnosis of appendicitis, or simulate intestinal obstruction. Localized pain, slight fever, and moderate leucocytosis may be present. The history, the presence of a blue line on the gums, and the blood changes are of importance in differential diagnosis."

"The cerebral symptoms are numerous. Seven of our cases showed marked cerebral involvement. One had delusions and maniacal excitement and had to be removed to an asylum. In other cases there occurred transient delirium, attacks of unconsciousness, and in one case convulsions. Optic neuritis or neuro-retinitis may occur. Hysterical symptoms occasionally occur in girls. Convulsions are not uncommon, and in an adult the possibility of lead-poisoning should always be considered. True epilepsy may follow the convulsions. An acute delirium may occur with hallucinations. The patients may have trance-like attacks, which follow or alternate with convulsions. A few cases of lead encephalopathy finally drift into lunatic asylums. Tremor is one of the commonest manifestations of lead-poisoning."

IV. EXPERIMENTAL

A. Materials

The sample of lead tetra ethyl, $Pb(C_2H_5)_4$, used was furnished by the Du Pont Company. It was a transparent, pale amber colored, volatile liquid, purity 95. per cent. The impurities were olefines. It decomposes at $120^\circ C$. and is soluble in alcohol, ether, ethyl bromide and gasoline. It is stable toward water but decomposes in direct sunlight, and was stored in a dark bottle in a closet.

B. Methods and Results

LOCAL APPLICATION.--Guinea Pig. This test whereby a definite amount of the compound is applied directly to the skin of the animal, depends upon absorption by the skin for its toxic effects. The guinea pig's chest and abdomen were shaved and cleansed 24 hours before applying the compound. The pig was strapped to an operating board and the compound was gradually applied to the skin from a pipette. The animal was allowed to remain on the board until all trace of the compound was absorbed. The time required for absorption was 20 minutes. The animal was then removed and placed in the hospital where symptoms were noted. The results follow:

<u>Amount applied</u>	<u>Weight of pig</u>	<u>Results</u>
1 cc	576 grams	Died 12 hours
1 cc	600 "	" 82 "
1 cc	626 "	" 26 "
0.75 cc	606 "	" 60 "
0.5 cc	520 "	Lived
0.6 cc	490 "	Died 36 hours
0.3 cc	502 "	" 60 "
0.3 cc	400 "	" 24 "
0.3 cc	420 "	" 18 "
0.2 cc	500 "	Lived
0.2 cc	406 "	"

The average weight of three pigs receiving 0.3 cc. was 440 grams. The lethal point by local application for guinea pigs is therefore placed at 0.6 cc. per kilo.

Symptoms: The first few hours after the application was made the pigs appeared normal. With the superlethal application (1 cc) two hours after exposure, marked depression was noted. This was quickly followed by body tremors. In four hours time the animal was helpless, the body and extremities trembling violently. Death followed in six hours. At the lethal point (0.3 cc) the symptoms were the same as described except the onset of the symptoms and death were delayed a little longer. These guinea pigs exhibited signs of pain and tenderness on pressure over the abdomen. After death the area of application appeared normal. There were no signs of excitement noted.

LOCAL APPLICATION.--Dogs. Local applications were made upon six dogs, the lead tetra ethyl being applied to the previously shaved thorax and abdomen. The results follow:

<u>Amt. applied</u> <u>per kilo body wt.</u>	<u>Results</u>
0.6 cc	Died 24 hours
0.5 cc	" 30 "
0.5 cc	" 73 "
0.3 cc	" 180 "
0.25 cc	Recovered
0.2 cc	"

The lethal point by local application for dogs was placed at 0.3 cc. per kilo body weight.

Symptoms: The symptoms following skin application to dogs were similar to those described for guinea pigs. When the animal received a lethal dose, it required about half an hour for complete absorption. The dog was then released from the board and placed in a large cage where he could be observed. The dogs gave prompt evidence of distress and abdominal pain, circling about the cage, sitting down and at once getting up as though it was impossible to reach a comfortable position. In several instances this period of uneasiness was followed by a profuse bowel discharge, the faeces being followed by watery fluid. After this the dog appeared easier and would lie down. Later the animals were depressed and comatose, but the belly was hard and rigid and pressure caused intense pain. On the second day the condition was much the same, except that the animal could only get on its legs with

difficulty. The entire belly wall was tense and rigid and the abdomen was very tender to pressure. Later trembling of the limbs occurred, followed by convulsions, collapse and death. In the case of sublethal doses, the symptoms were all milder and gradually disappeared as the animal returned to normal.

Pathology: Autopsies were performed on four dogs dying after having skin applications of lead tetra ethyl.

The external appearance and body cavities were normal, except in one case. In this case necropsy was performed immediately after death which occurred 75 hours after the application. Gas escaped as soon as the abdominal wall was opened, and the small and large intestines were acutely inflamed, probably as the result of perforation of one of the numerous ulcers. In all four cases the heart, lungs, spleen and liver showed no change but there was a mild congestion in all zones of the kidney. One case had a normal intestinal tract. In three cases there were ulcers throughout the intestines. These were in the region of Peyer's patches which were swollen and prominent. The ulcers were 1 or 1.5 cm. in diameter, punched out in appearance with clean cut edges and a smooth base with very little necrotic tissue in connection. The ulcer extended to the muscle layer undermining the mucosa slightly at that point. There was a large amount of blood in the lumen of the intestines in the three cases. One case had a small ulcer near the pyloric end of the stomach resembling the intestinal ulcers but much smaller in diameter. In the other cases the mucosa of the stomach was normal.

From both the symptoms observed when living and the pathological findings, it is evident that when lead tetra ethyl is applied locally near or over the abdomen, the lead acts directly on the intestines producing acute lead colic followed by ulceration which may lead to peritonitis. This confirms the observations of Oiler concerning cases of colic in ordinary lead poisoning which present the features of an acute intra-abdominal inflammatory condition.

LOCAL APPLICATION.—Cumulative Effects. A test was made upon a dog weighing 4.08 kilos, applying 0.1 cc. every twenty-four hours to a shaved area upon the chest, to ascertain the cumulative effects of the compound. The first ten 0.1 cc. applications did not affect the dog

appreciably. After the twelfth application the dog began to show depression and occasionally some nervousness. After the eighteenth application the dog was markedly depressed also very unsteady upon its feet and the trembling of the body showed marked increase. The trembling gradually increased until the twenty-first application had been made, the dog dying forty minutes after. No excitement was noted.

SUBCUTANEOUS INJECTION.—Guinea pigs. Two tests were made by subcutaneous injection. The pure compound was drawn into a hypodermic syringe and injected under the skin of the animals. The results follow:

<u>Amount Injected</u>	<u>Weight of animal</u>	<u>Results</u>
0.25 cc	510 grams	Died 164 hours
0.1 cc	580 "	" 96 "

Symptoms: The symptoms were similar to those noted under local application. The area of injection after death appeared normal.

SUBCUTANEOUS INJECTION.—Cumulative Effects.—Guinea Pigs: 0.01 cc. in pure olive oil injected every twenty-four hours. Three guinea pigs were selected for this test. Care was used to select pigs of the same weight. The results follow:

<u>Amount Injected</u>	<u>Average weight of pig</u>	<u>Results</u>
.01	640 grams	0/3
.01	640 "	0/3
.01	640 "	0/3
.01	640 "	0/3
.01	640 "	1/3
.01	640 "	2/3
.01	640 "	2/3
.01	640 "	3/3

Symptoms: The first three injections did not appreciably affect the animals. Six hours after the fourth injection one pig showed marked body tremors, while the other two pigs were markedly depressed. One pig died sixteen hours after the fourth injection. Six hours after the fifth injection the second pig was seized with body tremors and died after twenty hours. One pig survived for the eighth injection dying twenty-two hours after. There was no marked excitement noted.

INTRAVENOUS INJECTION.--Dogs. Five dogs were used in this test. Pure olive oil was used as diluent for the compound. The results follow:

<u>Amount injected per kilo body weight</u>	<u>Results</u>
0.078	Died 14 hours
0.039	" 14 "
0.011	" 25 "
0.0085	" 336 " (delayed)
0.0085	Lived

The lethal point for intravenous injection for dogs is placed at .011 cc. per kilo body weight.

Symptoms: Dogs injected intravenously showed almost immediate and marked symptoms from the compound. Five minutes after being injected there were marked twitching of the face and eyes, lachrymation of the eyes and nose, and rapid breathing, followed by marked excitement lasting for one hour to two hours. During the first hour after the injection animals vomited blood stained mucus and diarrhoea was also produced. The ejection from the bowels however did not appear blood stained. The excitement may have been caused partly by colic. The stage of excitement was followed by collapse, the dog becoming helpless with marked trembling of the body and extremities until death.

INHALATION.--Mice. A number of tests were run on mice by the continuous flow method to determine the toxicity of the compound by inhalation. Ten minute exposures to a gas air mixture of the compound were made, five mice being used for each concentration. The average weight of the mice was twenty grams. The construction of the mouse chamber will be found in report R.A.M.R.D. #11. The results follow:

<u>Concentration</u>	<u>Acute death</u>	<u>Delayed death</u>
5.598	4/5	0/5
5.11	5/5	0/5
4.958	0/5	0/5
4.166	0/5	0/5
3.679	0/5	0/5
3.617	0/5	0/5
3.425	0/5	0/5
2.812	0/5	0/5
1.615	0/5	0/5
0.71	0/5	2/5

The lethal concentration for mice by inhalation is placed at 5.11 milligrams per liter.

Symptoms: The mice showed activity while being exposed to the gas air mixture of the compound. Upon removal from the gas chamber the mice were markedly excited. In the case of lethal doses the excitement gave way to marked depression followed by collapse, trembling and death.

INHALATION. Cumulative Effects.--Mice. Mice showed the cumulative effects of the compound. Ten mice were subjected to concentrations of 0.5 milligrams per liter for ten minutes once every twenty-four hours, the sample being changed for each run. After the fourteenth run there was one death resulting from the compound. The fifteenth run produced two deaths, the nineteenth run one death and the twentieth run one death. The total number of experiments made was thirty-two, resulting in five deaths from ten mice used. The results follow:

<u>Date</u>	<u>No. of Mice</u>	<u>Concentration</u>	<u>Results</u>
5-27-24	10	0.49	0/10
5-28-24	10	0.49	0/10
5-29-24	10	0.438	0/10
5-30-24	10	0.392	0/10
5-31-24	10	0.497	0/10
6-1-24	10	0.473	0/10
6-2-24	10	0.458	0/10
6-3-24	10	0.462	0/10
6-4-24	10	0.481	0/10
6-5-24	10	0.505	0/10
6-6-24	10	0.438	0/10
6-7-24	10	0.5	0/10
6-8-24	10	0.532	1/10
6-9-24	9	0.47	2/9
6-10-24	7	0.626	0/7
6-11-24	7	0.548	0/7
6-12-24	7	0.604	0/7
6-13-24	7	0.564	1/7
6-14-24	6	0.643	1/6
6-15-24	5	0.534	0/5
6-16-24	5	0.545	0/5
6-17-24	5	0.479	0/5
6-18-24	5	0.419	0/5
6-19-24	5	0.5	0/5
6-20-24	5	0.486	0/5
7-1-24	5	0.437	0/5
7-2-24	5	0.494	0/5
7-3-24	5	0.563	0/5
7-4-24	5	0.543	0/5
7-5-24	5	0.521	0/5
7-6-24	5	0.593	0/5
7-7-24	5	0.594	0/5

Total number of runs made were 32. The average concentration was 0.5 milligrams per liter. The total deaths were five out of ten mice used.

Symptoms: The symptoms produced are the same as those recorded for mice.

Metabolism: If we assume, as is indicated by the symptoms, that the toxicity of lead tetra ethyl is due to the lead atom rather than the entire molecule, a study of the metabolism is of especial interest as showing a new form of acute lead poisoning. For we are dealing with a highly lipid soluble lead compound which is capable of skin penetration and which, furthermore, is comparatively stable. It is probable the only compound where acute lead poisoning follows absorption through the skin.

In chronic lead poisoning the skeleton of the body has been shown to be the storehouse for the comparatively large amount of lead accumulated. In acute lead poisoning distribution is throughout the body with the urine and faeces as the sources of elimination. Elimination through the faeces takes place even when absorption is through the respiratory tract, probably by excretion from the liver along with the bile.

A number of analyses were made on organs from both dogs and guinea pigs of which the best example is the systematic study of dog 1682 as given below:

Dog 1682

Weight 17.7 kgs. Given a skin application of 0.25 cc. lead tetra ethyl per kilo body weight, equivalent to 4.42 cc. or 7.97 mgms on August 12, 1914.

Days after Application	Urine Volume cc.	Lead Content mgs.	Faeces wt. grams	Lead Content mgs.
1	600	2.04		
2	330	1.32	35	15.5
3	340	1.09	5	3.0
4	150	0.8		
5	135	0.6		
6	165	0.5		
7	none			
8	280	0.6		

The dog was killed and autopsied on the eighth day.

	Mgs. lead per 50 Gram sample	Weight of Organ in grams (approx.)	Total lead in Mgs. (approx.)
Brain	1.8	75	2.7
Bone	5.0	2000	200.
Intestines, small	4.8	1000	96.
Intestines, large	5.3	20	2.1
Kidney	5.8	50	5.8
Liver	7.6	500	76.
Lung	4.2	200	16.8
Skin, area of application	25.2	1000	504.
Spleen	3.4	50	3.4
Total			906 mgs.

It is seen that approximately one fifth of all the lead applied was found in organs and tissue representing one quarter the total weight of the dog. The amount excreted was very small, amounting to only about one per cent of the total applied.

In a number of other animals that had received small doses some time before being killed, in the analysis of their organs no trace of lead was found. This would indicate that the lead was removed from the body tissues and deposited, probably in the skeleton.

Since the amount of lead excreted in the faeces and urine is very small, it is easy to understand how small amounts of lead tetra ethyl may have a cumulative action. The differences in individual susceptibility to this cumulative action are probably to be explained at least partially by the different rates of excretion of lead by different individuals. It is evident from the very small lethal dose by intravenous injection (0.011 cc.), that very small amounts of lead in the circulating blood are productive of serious disturbance of the nervous system, and also have a direct effect upon the intestines producing lead colic or even ulceration. These results of the acute action of lead are precisely similar to the symptoms of chronic intoxication, except that they are much more violent.

PROPHYLAXIS: Counteracting the effects produced by skin application. Chemical agents were used to counteract the effects produced by applying lead tetra ethyl to the skin. In these tests a lethal dose was applied and the chemical agents applied immediately afterward. Hydrochloric acid in strengths of 10%, 25%, 50%, and 60% were used and found to be valueless. Calcium Hypochlorite was used both in the form of a dry powder and paste and was found to have no value.

The Value of Solvents in Removing Lead Tetra Ethyl: A number of solvents were used to remove the lead tetra ethyl before a sufficient quantity to produce death was absorbed by the skin. In the following experiments the animals used were guinea pigs. The amount of lead tetra ethyl applied was a superlethal dose (1 cc.). The results follow:

Experiment #1 - Olive Oil

Two pigs were cleansed with olive oil one minute after application of lead tetra ethyl. Both pigs died.

Experiment #2 - Ordinary Soap and Water

Two pigs were cleansed with ordinary soap and water one minute after the application of lead tetra ethyl. Both pigs died.

Experiment #3 - Tincture Green Soap

Two pigs were cleansed with tincture green soap and water one minute after application of lead tetra ethyl. Both pigs lived.

Experiment #4 - Tincture Green Soap

Two pigs were cleansed with tincture green soap and water two minutes after application of lead tetra ethyl. Both pigs lived.

Experiment #5 - Tincture Green Soap

Two pigs were cleansed with tincture green soap and water five minutes after application of lead tetra ethyl. Both pigs died.

Experiment #6 - Kerosene

Two pigs were cleansed with kerosene one minute after application of lead tetra ethyl. Both pigs lived.

Experiment #7 - Kerosene

Two pigs were cleansed with kerosene five minutes after application of lead tetra ethyl. Both pigs lived.

Experiment #8 - Kerosene followed by Tincture Green Soap and Water
Two pigs were cleansed with kerosene which was followed by tincture green soap and water ten minutes after application of lead tetra ethyl. Both pigs lived.

Experiment #9 - Kerosene followed by tincture Green Soap and Water
Two pigs were cleansed with kerosene followed by tincture green soap and water fifteen minutes after lead tetra ethyl application. Both pigs lived.

Experiment #10 - Kerosene followed by Tincture Green Soap and Water
Two pigs were cleansed with kerosene followed by tincture green soap and water twenty minutes after application of lead tetra ethyl. Both pigs lived.

Experiment #11 - Kerosene followed by Tincture Green Soap and Water
Two pigs were cleansed with kerosene followed by tincture green soap and water twenty-five minutes after application of lead tetra ethyl. Both pigs lived.

Experiment #12 - Kerosene followed by Tincture Green Soap and Water
Two pigs were cleansed with kerosene followed by tincture green soap and water thirty minutes after application of lead tetra ethyl. One pig lived. One pig died.

Experiment #13 - Kerosene followed by Tincture Green Soap and Water
Four pigs were cleansed with kerosene followed by tincture green soap and water. Two pigs were cleansed thirty-five minutes after exposure. Two pigs were cleansed forty minutes after exposure. All four pigs died.

Conclusion: Both olive oil and common soap and water proved valueless as agents to remove the lead tetra ethyl from the skin. Tincture green soap was effective if used within two minutes after the application of the lead compound. Kerosene proved to be the best agent tried, all pigs lived that were kerosene treated up to thirty minutes. It was observed that the skin of the pigs that were treated with kerosene alone became tense, interfering with the movements of the animals. The skin would also crack and tear causing great discomfort. It was found that following the application of the kerosene by tincture green soap and water removed the kerosene leaving the skin soft and pliable.

V. DISCUSSION.

It is quite evident from these observations that the manufacture, handling and distribution of lead tetra ethyl involves considerable danger to operatives of acute lead poisoning in those instances where considerable material is splashed upon the skin, and of chronic lead poisoning from the absorption of small amounts by inhalation, by the skin or by mouth. Tests by the Bureau of Mines appear to show that lead tetra ethyl in exhaust gases of automobiles is not toxic to animals having been changed to insoluble forms of lead.

It is not believed that this compound is of any great value as a warfare agent because of its low toxicity as a vapor, and the fact that it decomposes at 120°C. Although splashes of this liquid on the skin will produce death, if toxicity for man is similar to toxicity for dogs it would require 21 cc. to cause the death of a man. Thus it could hardly be used as a spray for lethal effect although possibly a certain number of casualties could be so produced.

Submitted by:

W. A. Eldridge
W. A. Eldridge.

Supervised by:

D. C. Walton
D. C. Walton,
Lt. Cmdr., M.C., U.S.N.,
Chief, Dep't. of Toxicology.

Approved by:

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

A Study of the Toxicity of
Lead Tetra Ethyl.

Work begun: May 7, 1924.
Work completed: October 5, 1924.

(8 copies made)
(copied; 4f)