in the body of every animal that died. I might say at this point that we did not have the experience that Doctor Sayers and Doctor Kehoe had—that of finding lead in the body of our normal animals.

We kept our control animals upstairs in another room where there was no chance for them to come in contact with the lead compound. I would also like to say that the normal man does not contain lead in his body as commonly as some people think. I examined the stools of many of the men exposed at the Bayway plant and was able to find lead in the stools of only 18 or 19 cases out of the 28 examined. Also in the past year we have had in our hands records of the urine and blood findings of, I should think, 500 men. Over 300 of these men were employed by the National Lead Co., and concerns in similar lines of business and the records show that lead was found in the urine of only 20 per cent of the men. Of course the exposure of these varied. The stippled cell findings in these cases was rather rare also, but this is in agreement with the literature. We ourselves have examined the urines of several hundred men during the past year and found lead only in about 30 per cent.

For fear that we might have some mistake in our lead chamber and because the question arose as to whether lead, or rather the tetraethyl lead, evaporated with the gasoline we decided on further experiments. We took a galvanized iron pan 30 inches in diameter, having a depth of 20 inches, and placed a movable false bottom of ½-inch mesh screen 11 inches from the bottom. Each morning we poured a liter and a half of ethyl gasoline on the bottom of the pan after it had been thoroughly cleaned and dried. The movable false bottom was then placed in position and on it were placed 10 rats. The top of the pan was left open to the natural air movement, except for a ½-inch mesh screen placed over the top to keep the rats from jumping out. The rats were exposed to the fumes resulting from the natural evaporation of the gasoline for 22 hours daily for 7 days.

For two hours each day the rats were removed to give them a chance to eat and drink and to permit us to clean out the pan. It was observed that approximately 200 cubic centimeters of gasoline were left unevaporated at the end of the 22 hours. At the end of the seven days the rats were killed and examined. An average lead content of 4 milligrams per rat weighing 150 grams was found. There was no way that the rats could have come in contact with any lead except through the fumes formed by the natural evaporation of the ethyl gasoline. There was no dust as the bottom was still moist. We feel after this experiment that there can be no doubt in our minds that the lead concentration in the ethyl-gasoline fumes is of sufficient degree to cause lead storage in the body in appreciable quantity. Of course, we are not claiming that man has the same exposure that these animals have had. No one expects a man to be

standing over a pool of gasoline for 20 hours a day. It has been stated that a man retains 80 per cent of the gasoline that he breathes into his lungs. If this is so there can be no doubt that he runs a chance over a long period of time of accumulating an appreciable quantity of lead. The thing to remember is that lead is an accumulative poison, while such poisons as carbon monoxide or benzol are washed out of the system when the exposure is over.

There is one interesting fact, which has had some newspaper notoriety, I believe, in some parts of the country. Two persons working with all the care they could in making this investigation have shown lead absorption. These persons were not exposed to any straight tetraethyl lead except to very small amounts and then for only a couple of minutes a day. I do not believe they had what we would call lead-intoxication symptoms—I would hesitate to say that. They showed wakefulness at night and irrational dreams, etc., but the fact that they accumulated lead under those conditions shows that lead could be absorbed under ordinary conditions around garages. Our windows were kept wide open and the ventilation in our experimental room was as good as one would find in such places.

Our experience leads us to believe that if man is given the same exposure that our animals have had that he can not help but absorb lead, whether it be through the skin or by means of the lungs. Whether the symptoms are well enough known for the average practicing physician to recognize is a question. Even an autopsy fails to give conclusive indications. We have sent animals to the Presbyterian and Bellevue Hospitals and have asked them to make an examination for us. Each time we have got back a report that there is nothing significant. One animal, on which the Presbyterian Hospital made a special examination of the nervous system, was reported on the other day, and lesions of the brain were noted, but the report closed with the remarks: "These lesions are no more than we find in 50 per cent of our animals." We find that an autopsy of the men who died at the Reconstruction Hospital revealed practically nothing that would indicate lead poisoning, except from the chemical findings and the fact that it was known where the men worked. We have had the same experience with our animals. Our leaded animals showed nothing that was not observed in a certain percentage of normal animals. All we have to go on, except for the rare animal, was the fact that we found lead in the excretion, lead in body after death, and stippled cells in about 50 per cent of the animals. Thus our animal work checks the findings on man.

The CHAIRMAN. Has anybody else anything to add? Doctor Thompson, you probably know of some one who has something to say along this line.

Doctor THOMPSON. I suggest Doctor Kehoe.

DR. ROBERT A. KEHOE

College of Medicine, University of Cincinnati, Cincinnati, Ohio

Mr. Chairman and gentlemen, I have here quite a mass of data which I will not inflict on you at this time. There are a number of items here of experimental work that we have carried out during the course of the past year. The first of these refers to the actual toxicity of tetraethyl lead. Since this is not germane to the subject under discussion, I should like to omit reading it, except to point out one thing. We carried out this study, not only with the tetraethyl lead, but with certain other compounds of lead as well, the chloride and nitrate, and compared their toxicity. It is worth while to say at this time that, considering those manners of absorption which are common to both, the toxicity of tetraethyl lead is of the same order and magnitude as that of ordinary lead compounds. The only difference in the toxicity of the two lies in the fact that the one, tetraethyl lead, is capable of being absorbed through the skin. I should like to bring that out, in order to show that their toxicity is practically identical. The data are presented in this paper covering the actual toxicity of tetraethyl lead with regard to rabbits only.

The toxicity of tetraethyl lead for rabbits has been determined for the various methods of administration, and it has been compared with the toxicity of certain inorganic salts of lead. In the case of both tetraethyl lead and the inorganic salts of lead a sufficient number of animals have been studied to make possible a proper allowance for individual variation. If only the lethal amount for a single administration be considered, little individual variation is seen. However, if the toxicity be considered on the basis of numerous repeated administrations, a considerable variation is found.

The fatal dosages of tetraethyl lead administered in one dose to rabbits by various means are substantially as follows: Intravenously, 0.014 cubic centimeter per kilo body weight, approximately 0.014 gram lead per kilo; cutaneously, 0.7 cubic centimeter per kilo body weight, or about 0.7 gram lead per kilo; by oral administration, 0.11 cubic centimeter per kilo body weight, or about 0.11 gram lead per kilo; the quantity taken into the body of the animal by inhalation is difficult to calculate for a variety of reasons, but the concentration of tetraethyl lead in terms of lead in the air breathed by the animal which will kill in about three days of six-hour daily exposure is approximately 0.182 milligram per liter of air.

In all of these methods death of the animal takes place in from 6 to 72 hours.

The fatal dosages of salts of lead, such as the chloride and nitrate, are not widely variant from the above figures.

When lead chloride is administered intravenously a variety of ings may occur, dependent upon the salt employed, the speed of ministration, and the concentration of the solution. The animal y die at once, may develop a thrombosis at the site of the injec- n, or may develop a general systemic poisoning. The lethal dosage calculated, on the basis of the last situation, to be about 0.015 gram lead per kilo.

When administered orally approximately 0.037 gram of lead per lo is required to produce death from one dose.

In the case of lead nitrate approximately 0.011 gram of lead per lo injected intravenously brings about death within 24 hours.

The cutaneous application of inorganic salts of lead results neither death nor illness of the animals.

Comparison of the toxicity of tetraethyl lead with that of the organic salts of lead shows that in general these are of the same der of magnitude. An exception of sufficient magnitude to be well tside the limit of chance variation is seen, however, when one mpares the poisonous character of lead salts taken by mouth with t of tetraethyl lead taken in the same way. In this case the salts lead are seen to be about three times as toxic as tetraethyl lead. is is probably due to the greater ease of absorption of lead salts in e alimentary tract. On the other hand, lead salts are not absorbed lethal doses from skin, whereas death may readily be produced by e application of tetraethyl lead to the skin.

The general conclusion which seems to be obvious from the data en above is that tetraethyl lead owes its toxicity to the lead and t to any other part of the compound. Furthermore, it is plain t the compound, tetraethyl lead, is not peculiarly toxic as com- red with other heavy metal compounds, but that its principal nger resides in the fact that it is readily absorbed through the n, as well as being capable of inhalation because of its volatility.

When tetraethyl lead is administered in smaller repeated doses, e outcome is dependent upon the size of the dose and the time erval between doses. In a series of rabbits treated with 0.1 cubic timeter at intervals of three days, symptoms began to appear most cases after 6 or 8 treatments. (The only symptom was a ght loss of weight.) The total quantity applied before the death these animals averaged about twice the amount of a single lethal e. It will be seen from the consideration of later experiments t the lethal amount is dependent not so much on the total quan- y of lead which the animal is led to absorb, but rather upon the centration actively mobilized (in the blood stream probably) at particular time.

The accumulation of lead in exposed animals treated with sublethal doses was also made an object of study. This is only of importance in pointing out that in sublethal dose lead is cumulative.

There are one or two items of value in this which it is worth while to point out. A considerable interval of time elapses between the period of the last dose applied to the animal and the period of analysis; the quantity of lead found in the animal is surprisingly low compared with the animals analyzed immediately following the last dose. In order to make that point clear, I should like to present a little of our data.

In the table given may be seen observations and analytical data collected on a series of nine rabbits treated at intervals of three days with 0.1 cubic centimeter of pure tetraethyl lead, applied to the skin of the abdomen.

These rabbits varied in weight slightly, running from 2½ kilos to a little less; in other words, they were approximately the same size. The number of their treatments varied as follows: 16 treatments, 13 treatments, 15, 17, 7, 14, 14, 11, and 10. That is to say, one of these animals received 16 treatments of 0.1 cubic centimeter of tetraethyl lead applied to the belly. Of these animals 3 have survived, and, so far as could be seen, developed no symptoms. The others died at variable periods of time. One of them died 23 days after his last treatment and contained 15.3 milligrams of lead. Another died the day after his fifteenth treatment, and this one had 96 milligrams. Several other animals are presented in the same way, and they show the same thing. That is, if the animal happens to be analyzed immediately after he dies, he has lead in him as a result of that treatment anywhere from 50 to 96 milligrams; if the animal be analyzed two or three weeks after the last treatment, as some of these animals were, the quantity of lead which is found in them varies from 7 to 15 milligrams.

Rabbit	Weight	Number of treatments	Time of appearance of loss of weight	Result	Lead determination in milligrams
	Pounds				
No. 31	5⅜	16	Seventh treatment.	Died 23 days after last treatment	15.3
No. 34	6⅛	13	No loss of weight	Same	9.78
No. 35	6	15	Eighth treatment	Died day after fifteenth treatment	96.0
No. 36	5¾	17	Fourteenth treatment.	Survived	
No. 37	6¾	7		Died after seventh treatment	90
No. 39	4⅞	14	Seventh treatment.	Died 29 days after last treatment	7.10
No. 40	4½	14	do	Survived	
No. 42	4⅝	11	Ninth treatment	Died after eleventh treatment	51.25
No. 60	3½	10	Seventh treatment.	Survived	

This factor of variation puzzled us somewhat, because these animals were of the same general condition of health, approximately the same size and age, and it would seem they should have absorbed somewhat more nearly the same quantity, although there would, of course, be some allowance for individual variations. It appeared, however, that this variation is probably due to the rate of secretion. Lead from these animals and the rate of secretion in these animals was of such an order of magnitude as to lead one to question the toxicity of a compound of lead different from that ordinarily occurring in lead poisoning, and this question is presented the more strongly when the rate of excretion of lead in men poisoned by tetraethyl lead is studied.

The excretion of some of these animals was observed. They were put in an ordinary cage and their urine and feces were collected over periods of seven days in order to give a considerable amount of material, so as to avoid an experimental error, and careful analyses were made. The quantity of lead secreted by these animals, and these represent animals of this same group of which I spoke, was as follows:

Rabbit	Period of collection	Quantity of lead, in milligrams
	Days	
2 controls	7	Nil.
No. 31 [1]	7	5.89
No. 36	7	4.00
No. 39	7	2.08

[1] This animal died Dec. 21. His entire body contained 15.3 milligrams of lead. Some idea can be obtained of the quantity of lead in the body of this animal at a time when he was excreting almost 1 milligram per day.

This gives an idea of the quantity of lead which in the body of an animal gives rise to an excretion of about a milligram per day.

This fairly rapid rate of excretion raises the question as to whether in the decomposition of the tetraethyl lead molecule a compound of lead may not be formed which is more readily excreted than the ordinary compounds of lead. This question is presented the more strongly when the rate of excretion of lead in men poisoned by tetraethyl lead is studied.

The distribution of lead in poisoned animals.—A number of animals known to contain considerable quantities of lead at the time of death were analyzed after the separation of their tissues. The data below indicate the manner of poisoning of the animal, together with the lead content of various tissues.

Rabbit No. 32.—Exposed for 72 days to vapor of Pb $(Et)_4$ in air at the rate of 100 cubic centimeters PB $(Et)_4$ vapor to 5 liters of air.

Tissue	Weight	Lead in milligrams
	Grams	
Bones	225	9.15
Skin	300	3.18
Liver and kidneys	56	3.70
Central nervous system	13	Nil.

This animal had two young in the uterus at the time of her death, or several—I do not remember how many there were, but their entire weight was 126 grams, and they contained 0.28 milligram of lead. The other tissues weighed 2,045 grams and contained 8.75 milligrams of lead.

Note: One liter of saturated vapor of Pb $(Et)_4$ at 25° C. contains 0.00456 gram Pb.

In these cases, and after this long period of exposure, we find that considerably more than half of the lead in the animal was distributed in parts other than the bones.

Rabbit No. 31.—Treated every three days with 0.1 cubic centimeter Pb $(Et)_4$, 16 treatments. Died 23 days after last treatment.

Tissue	Weight	Lead, in milligrams
Bones	325 grams	8.04
Skin	260 grams	4.49
Liver and kidneys	105 grams	1.15
Central nervous system	13.5 grams	(1)
Other tissues	1,590 grams	2.02
Urine in bladder	50 cubic centimeters	0.14

1 Lost in analysis.

We were at that time working on some theoretical notions of our own with regard to the materials which bring about increases in rate of secretion from poisoned animals, and this animal at this time had this quantity of lead in its urine, which I have no doubt is a very unusual quantity.

Rabbit No. 16.—Exposed for 98 days to vapor of Pb $(Et)_4$ in air at rate of 5 cubic centimeters of Pb $(Et)_4$ vapor to 5 liters of air, and then for 3 days to 200 cubic centimeters vapor in 5 liters of air. Died.

The bones of this animal contained 2.22 milligrams of lead, the liver weighed 82 grams and contained 3.75 milligrams, the central nervous system weighed 18 grams and contained 0.13 milligrams of lead, while the remainder, without the skin, weighed 2,160 grams and contained 26 milligrams of lead.

These data simply show that in these animals the distribution of lead is such as to show that not all the lead is stored in the bones. One wonders—and we are attempting to determine the point—whether the distribution of lead in experimental animals poisoned by tetraethyl lead is the same as that of animals which have been poisoned by ordinary lead compounds. That, of course, brings up the point, which can be seen at once, that when an organic compound such as tetraethyl lead is taken into the body its fate in the tissues can hardly be determined with ease, and one wonders what is the

exact nature of the decomposition. One thing is certain, the lead which appears in the urine and feces is in an inorganic form, but in exactly what state I am not able to say.

The pathology which has been observed in animals actually poisoned with tetraethyl lead may be a matter of some interest.

When toxic amounts of tetraethyl lead are administered to rabbits, the first symptoms seen are lack of appetite and loss of weight. A sluggishness and lassitude are apparent, and the animal sits with drooped ears and arched back. As the symptoms increase in severity, he becomes nervous, moving about in the cage from place to place, stopping from time to time to sink into a drowsy state. The temperature does not ordinarily vary more than is normal in these animals, but respiration quickens at first and then, with increasing severity of symptoms, decreases. If sufficient time intervenes before death, a watery diarrhoea develops. Convulsions usually occur as a terminal sign, and the animal dies, with bulging, congested eyes and paralyzed respiration, with the heart continuing for some time afterward. When illness results from inhalation there is an irritation, with some weeping of the mucous membranes. The upper respiratory tract may become red and in very severe cases even hemorrhagic. When the application is made on the abdominal wall there is an almost immediate increase in the peristaltic activity of the intestines. Rapid peristalsis may be easily observed under the abdominal wall. During the course of their illness, whether acute or prolonged, no characteristic objective signs develop. There is no typical alteration of the blood picture. (Stippling and polychromatophilia are found frequently in normal rabbits, so that no minute changes would be demonstrable.) Only a slight anemia has appeared in any experimental animal thus far.

We found, as a matter of fact, in the cases a considerable number of normal rabbits which we had at our disposal at the University of Cincinnati, where there was no possible exposure to lead, that a very large number showed stippling and polychromatophilia. We therefore came to the conclusion that a change of this sort in the blood is very likely to be of questionable importance.

Post-mortem examination of poisoned animals discloses certain characteristic, though not definitely differentiating, changes. These are confined almost wholly to the alimentary tract and the central nervous system. There is a considerable amount of capillary dilatation of the viscera generally, and the heart is usually dilated and flabby, but the pronounced findings are seen in an acute intestinal irritation and desquamation and an acute edema of the brain. The intestinal change is confined almost wholly to the small intestine and is most pronounced in the duodenum. Here the intestine is filled with a sticky mucoid fluid which may be, but usually is not, blood tinged. It is characteristically yellowish and glairy, and often coagulates spontaneously on standing for a time. The mucosa in this region is thin and almost fluid in character. No actual ulceration is found, and there are seldom any definite hemorrhagic areas. The brain is either dry and swollen and very friable, or else it is very wet with a large amount of free fluid under the dura, especially at the base.

Microscopic findings are very meager. No characteristic change has been found. The study of microscopic pathology has not been completed.

Among the effects on experimental animals, which should be noted in passing, is the influence of lead poisoning on pregnancy and the procreative functions in general. A number of pregnant female rabbits have given birth to premature litters. In several cases abortion or miscarriage has resulted shortly after the administration of the poison. However, the loss of ability to reproduce has not occurred in the case of either male or female rabbits. Animals which have been severely poisoned have been both fertilized and become impregnated, and have brought forth normal young after only brief periods of recovery.

So far my entire discussion has referred to pure tetraethyl lead and has had nothing to do with the matter of gasoline. My next paper refers to the absorption of tetraethyl lead through the skin, and I am going to give you just a brief summary of it:

In the former experiments, in which the toxicity of tetraethyl lead as absorbed through the skin was determined, there was in almost every case a possibility that the animal had obtained a portion of the lead by inhalation and ingestion. It was determined, therefore, to carry out some experiments to control this factor and to establish, beyond any doubt, the facts in the matter.

For this reason animals of about the same size were selected, and several of them were exposed to a definite concentration of tetraethyl lead in gasoline in the following manner:

The animal had the hair clipped off of the fore foot, as well as could be done without any injury to the skin at all, then this fore foot was dipped up to the elbow joint in this solution of tetraethyl lead in gasoline, and was held there for the period of an hour in such a way as not to interfere with the circulation. During this period of time, in which we were working with concentrated solutions, a high rate of ventilation was maintained so the animal would have no opportunity of inhaling appreciable quantities of tetraethyl lead vapor. Briefly, the result of these experiments was as follows:

1. Three rabbits of approximately the same weight (about 2 kilos) were posed for half an hour each on three consecutive days to a 1 to 10 dilution tetraethyl lead in gasoline. Each animal was carefully tied down on a fortable board, as much as possible of the hair was clipped from a foreleg thout any abrasion, and the leg was gently but firmly held in a test tube the solution, down to the elbow joint. Care was taken not to interfere the circulation. The quantity of solution to which the leg was exsed was approximately 35 cubic centimeters. The exposure was carried in a hood where the air was being changed rapidly. At the end of the posure the leg was bathed in kerosene repeatedly, wiped dry, and then eated with cold cream, for the purpose of counteracting the harmful effect the gasoline on the skin.

At the end of three such treatments the animals developed paralysis of the d legs, and on the next day they died. Control animals, two in number, the same weight, treated in exactly the same manner except that the gasone contained no tetraethyl lead, showed no indication of injury beyond some gree of irritation of the skin.

One of the animals was ashed and an analysis for lead was made. The tire carcass contained 36.46 milligrams of lead. It is well to point out at this animal had been exposed for one and one-half hours to 105 cubic ntimeters of a solution containing approximately 10 grams of lead. Approximately 0.35 of 1 per cent was absorbed.

2. Ten rabbits were selected and were treated in the same manner, three ing used as controls and seven being exposed for half an hour at a time a dilution of 1 part of tetraethyl lead in 100 parts of gasoline. For the st seven days the treatment was carried out daily. After this the exposures were made twice weekly. This was done because of the skin irritation hich resulted from the daily treatment. It was found that the skin could kept intact by increasing the interval between exposures, provided the skin treated with cold cream in the interval.

The following table shows the results of such treatment:

Number of animals	Number of treatments	Weight		Result
		Before	After	
ontrol)	28	3¾	5⅛	Survived.
ontrol)	27	4¼	5⅛	Do.
ontrol)	27	3¼	3¾	Do.
1:100)	7	4¼	4⅜	Killed for analysis.[1]
1:100)	29	3¾	4¾	Survived.
1:100)	29	4¾	5⅛	Do.
1:100)	16	4¼	4½	Died suddenly without previous illness.[2]
1:100)	27	4¼	3½	Ill after tenth treatment. Recovered.
1:100)	25	5¼	6½	Survived.
1:100)	22	4	4½	Paralysis and death.[3]

Lead content of carcass of 90, 3.81 milligrams.
Lead content of carcass of 94, 7.50 milligrams.
No analysis was made of carcass of 97.

One of the animals received seven treatments and was killed for analysis this time in order to get data as quickly as possible. As will be noted, of remaining 6 animals 4 survived, 2 died; one of them died suddenly, without any evidence of illness, from a cause which could not be ascertained; other developed a paralysis which may have been due to the manner of tying on the board and which may have been due to the lead.

For our purposes it may be safe to assume both those animals died of lead poisoning. Of course the manner of taking a rabbit and tying him down to an animal board and keeping him there quietly for half an hour presents certain experimental difficulties of its own.

The above data show that there is an accumulation of lead in rabbits treated with gasoline containing a sufficient quantity of tetraethyl lead and that the animals may be poisoned by a concentration of 1 part tetraethyl lead to 100 parts of gasoline. It is of some importance to see that animals treated with a concentration of 1 part of tetraethyl lead to 100 parts of gasoline absorbed approximately one-thirtieth as much as animals exposed under identical conditions to ten times that concentration, i. e., 1 to 10.

The question, then, of the toxicity of ethyl gasoline arises. On one aspect of this matter Doctor Edgar has some experimental data which are worth while presenting to you, of the same general type as Doctor Sayers, showing the volatization of ethyl lead and gasoline. Leaving that out of the question for the moment, I should like to present some experiments we have done on the ethyl-gasoline work:

The question of the hazard existing in the handling of ethyl gasoline hinges upon two considerations: (*a*) whether the quantity of tetraethyl lead volatilizing out of gasoline at the existing concentration (1:1,300 approximately) is sufficient to cause appreciable absorption of lead; (*b*) whether skin absorption of tetraethyl lead in gasoline can occur to an extent sufficient to cause poisoning.

I should like to ask your permission to read this entire thing, because there are several details of it which I think are of rather vital importance.

Both of these problems were investigated by exposing animals to conditions as nearly like the normal conditions of human exposure as could be devised. For this purpose guinea pigs and monkeys were selected: guinea pigs, because of their susceptibility to lead poisoning, and monkeys because of their similarity to the human being.

The guinea pigs were divided into four groups, kept separate, but fed and cared for in exactly the same manner. Eleven pigs, four females and the remainder males, were treated on the skin surface of the belly, after clipping off the hair, with 1 cubic centimeter of ethylized gasoline. Eleven, all females, were set aside as untreated controls. Eleven, five of which were females, were treated with 0.2 cubic centimeter of ethylized gasoline. Three, one male and two females, were treated with 1 cubic centimeter of ordinary gasoline.

I might say that we took no precaution at this point, so far as the inhalation of the gasoline containing tetraethyl lead was concerned, nor did we attempt to take any precaution against the animals licking themselves, or others of their group. This we felt was, so far as the inhalation was concerned, only an addition to the excellence of the experiment and presented two hazards instead of one.

The gasoline used was a good grade of high-test commercial gasoline. The ethylized gasoline was prepared by first making a mixture of pure tetraethyl lead and ethylene dibromide in the proportion of three parts of lead to two parts of dibromide. This mixture was kept in a tightly sealed brown bottle to prevent decomposition, and was mixed in gasoline in quantities of 0.25 cubic centimeter to 200 cubic centimeters of gasoline, as needed. This corresponds to the most concentrated mixture of tetraethyl lead in gasoline, known as a 3 E mix representing approximately 1 part by volume of tetraethyl lead per 1,300 parts of gasoline.

The monkeys, four in number, of the Rhesus type, were all cared for in the same manner. Two were used for controls, and two were treated daily with 1 cubic centimeters of ethyl gasoline, prepared in the above manner. The hair was clipped from an area on the back, as large as the palm of the hand and the gasoline mixture was dropped on out of a pipette. One of the monkeys to be used as a control died within a few days after his arrival, having contracted pneumonia in transit. The other control escaped from his cage and died of exposure before he could be captured. The two being treated as above were continued without any controls for comparison.

The following paragraphs indicate the course of the experiments carried out upon these animals.

GUINEA PIGS

Pen No. 1.—Four females, seven males. Treatments twice weekly. Treated with 1 cubic centimeter ethyl gasoline. Number of treatments, 40.

In the period from November 25 to the present there had been no natural deaths among these animals. Three were killed for analysis on March 3, and one was killed for analysis on March 31. The females have given birth to young, which have survived, two of which were born May 14. There have been two litters of young born dead. These occurred in January and February, during periods of inclement weather, in which all of the animals suffered somewhat.

Two pigs were selected, because of distinctive markings, for observation of blood conditions. The initial observations on the two were as follows:

(*a*) Hb. (Dare method) 90, red count, 6,160,000.

(*b*) Hb. 110, red count, 5,200,000.

Observations made on May 17 were as follows:

(*a*) Hb. 90, red count, 5,754,000.

(*b*) Hb. 105, red count, 5,230,000.

The variations in these, as can be seen, are well within the limits of experimental error.

Blood smears show no appreciable change now as compared with the original observations. Guinea-pig blood under normal conditions shows a variable amount of polychromatophilia, and an occasional stippled cell may be found in the blood of a normal animal. In the two pigs above no stippling has ever been seen. Bluish or basophilic staining erythrocytes may be seen in almost every field. There has been no noticeable increase in the number of these.

Of the seven pigs remaining in this group two males do not appear to be in good condition at present. They have been fighting almost constantly lately and have inflicted many deep wounds upon each other, some of which are infected and suppurating. It has been thought advisable to segregate these animals and continue the experiment to see if healing of wounds will bring about recovery. The two females remaining look healthy and sleek, except for the irritation of the skin of the belly.

Pen No. 2.—Eleven females. Not treated. Male from pen No. 4 introduced. There have been no natural deaths among these animals. Three were killed for analysis March 3 and one was killed for analysis March 31. Forty young have been born alive, of which three have died within a few days of the day of their birth. Three females have given birth prematurely to young, one of these on May 13.

Two pigs were selected for their distinctive markings, and blood examinations were made as in the case of group No. 1. No variation was seen in the blood picture, and no variation as compared with those in pen No. 1 was seen, except that in one pig an occasional stippled erythrocyte was found.

These animals are in good condition and present no demonstrable deviation from the normal.

Pen No. 3.—Six females, five males. Treatments twice weekly. Treated with 0.2 cubic centimeter ethyl gasoline. Number of treatments, 40.

Since November 25, the beginning of the experiment, there have been no deaths among these animals as a result of illness. Three were killed for analysis on March 3. Twenty-four young ones have been born, of which 19 are now alive. The others died within a day or two of their birth. There have been three litters born dead. None of these occurred since April 1.

The blood findings in these animals are no more significant than those in the other groups of pigs. No variation from the normal has been found in spite of repeated examinations.

The animals are all healthy.

Pen No. 4.—One male, two females. Treatments twice weekly. Treated with 1 cubic centimeter gasoline. Number of treatments, 40.

There have been no deaths in this group. Two litters of young have been born, six young in all, of which one was dead at birth.

No blood examinations have been made on the pigs in this pen since the first examination. They were used largely as controls on the influence of the gasoline alone on the skin. No variation is seen either in the condition of their skin or their general appearance as compared to treated animals.

An unfortunate and unforeseen variable was found in the conduct of these experiments when a group of treated and control animals were killed for analysis on March 3. The table below shows the lead content of the carcasses of these animals. It will be seen that the quantity of lead is practically the same in all animals, treated and control alike. This was not due to any mistakes in handling or treating the animals, nor was there the remotest chance of incorrect selection of animals for analysis. The explanation can be found only in a detailed consideration of all the environmental factors. The first three groups of these animals were quartered in a single large pen, divided into three parts by wooden partitions of tongued and grooved siding. The top and front side were made of inch mesh wire netting. There was no chance, therefore, for the excreta of one group of animals contaminating the food of the others; nor could dust from one cage enter the other in considerable quantity.

I enumerate these things because in the handling of this type of volatile decomposing substances these matters are of the utmost importance in determining whether or not in a given animal you get a quantity of lead or none at all. Any variation in the manner of handling the animals from one of complete segregation leads to the accumulation of lead in control animals from unforeseen sources.

When the animals were received they were kept on the animal board until the treated surface was dry before being returned to the cages. No special ventilation was employed, since there was no objection in this case to inhalation of gasoline and tetraethyl lead vapor. (In the case of human exposure both of these possibilities are presented.) Under these conditions the opportunity for inhalation of vapor from treated animals was not presented to control animals.

The cause for the experimental result can be found only in a condition to which all of the animals were equally exposed.

These animals were moved in rather hurriedly when the weather became ad, and I suppose the rather hurried manner in which they were moved led s into error in the selection of a place for them.

One end of the large room, which was being used for housing the animals uring the cold weather, was used from time to time as a place of storage r returned packing cases filled with empty and full cans used for the early istribution of tetraethyl lead.

It is apparent, and should have been foreseen, that a quantity of the dust esultant from the decomposition of such a portion of tetraethyl lead as was eft in these cans accumulated on the floor of the room and was carried by urrents of air, and the feet of attendants, to that portion of the room used r the animals. It is almost certain that the food of the animals was conminated as well. In this manner the animals ingested and inhaled such antities of lead as to completely spoil the experiment.

Analytical results, March 3

Three guinea pigs, pen No. 1, 2.10–2.10–2.55.

Three guinea pigs, pen No. 2, 2.00–2.00–2.10.

Three guinea pigs, pen No. 3, 1.60–2.00. Beaker broken, analysis spoiled.

Analysis repeated March 31 as check

One guinea pig, pen No. 1, white buck, weight $1\frac{1}{16}$ pounds, 2.55.

One guinea pig, pen No. 2, white and black female, weight $1\frac{3}{16}$ pounds, 2.10.

This analysis was repeated a little later, as we wanted to be absolutely ertain of our experimental data and also wished to be certain of our nalytical method. I might say at this time that I think there can be no estion about the analytical method inasmuch as it was worked over by r staff under the direction of Doctor Edgar, and the method, we think, s as good as can possibly be devised for the determination of lead.

As a result of the error in the manner of conducting this experiment, no nclusions may be drawn as to the quantity of lead which may have been sorbed from the leaded gasoline. It may be of some significance, however, at the quantity of lead absorbed from the gasoline, if any, made no appreciable ference in the total lead obtained from all sources. Such variation as occurs the entire group of animals may be explainable on the basis of variations weight. It is certainly significant that even under these adverse conditions ere was no demonstrable evidence of the poisoning of any one of these anils, unless the miscarriages be considered. This is of extremely doubtful nificance, since such occurrences are not infrequent in a group of this numr of animals in any environment.

MONKEYS

Monkey No. 1.—Rhesus male. Weight $5\frac{1}{8}$ pounds, January 19. Treated th 2 cubic centimeters ethyl gasoline daily. Number of treatments, 88.

This monkey is now lively, apparently perfectly well, is tame, playful, and good condition in every way, except for some degree of irritation of the skin its back.

The second monkey was treated in exactly the same manner and showed tantially the same thing, so there is no need to repeat his story.

In April the animals concerned in the above experiments were moved into different quarters, which allow of no opportunity of exposure to lead in any way other than under controlled experimental conditions. Treatments are being continued to determine if symptoms and signs of poisoning can be produced by the experimental methods previously outlined.

The CHAIRMAN. I believe, if I can read your faces aright, this is the time to adjourn for lunch. We will meet again at 2 o'clock and complete the discussion.

(Thereupon, at 1 o'clock p. m., a recess was taken until 2 o'clock p. m.)

Afternoon Session

The CHAIRMAN. In accordance with the program, I suggest that we now take up the discussion of the experimental data which were reported this morning, and I am going to ask Doctor Henderson, of Yale, if he will open the discussion.

DR. YANDELL HENDERSON

Professor of Applied Physiology, Yale University

Mr. Chairman and gentlemen, I have no general paper to present, such as we have listened to this morning. There are, however, one or two quite general points that have occurred to me as this conference has gone on that I would like with your permission to mention before I touch on more specific matters. One point is that which Secretary Work spoke of, that we might be here for a number of days. I think I ought to say, on behalf of myself and my colleagues, that we can scarcely stay beyond to-day. We are down here on our own expense, neglecting work which we ought to do, and I hope this conference will finish this evening if possible. I think we ought to do so, and to set an example I am going to be very brief and merely try, as the chairman has suggested, to open this discussion.

There is one other point of a general character that I want to call to your attention. The Surgeon General, in opening this meeting, spoke of the lack of laws applying to such a matter as this, and, to my mind, there he touched on a matter which is more important by far than the specific question before us. As I understand it, the Surgeon General has neither authority to say that ethyl gas may be made or may not be made, or even to direct an investigation involving the expenditure of Government money without special act of Congress. I should like to point out that if gasoline were a food this situation would not exist. We have full legal protection and legal definition of foods and of their qualities, and it seems to me that this is one thing that we all can agree on. Perhaps the two sides here present will not be able to agree with regard to the par-

icular question of whether ethyl gasoline shall be used or not, but seems to me that we can all agree that such a situation as has risen regarding leaded gasoline should not arise again; that there hould be legislation to give the necessary power to the Health rvice. Then, when other questions of this sort come up, as they rtainly will, the Surgeon General would have full authority, just s the Bureau of Chemistry in the Department of Agriculture now as full authority over foods. The Surgeon General should have ull authority to investigate and supervise and to advise the public, e State boards of health, and city boards of health in all such atters. I have handed to the Surgeon General a resolution covering this idea. I do not think we are at a point in the discussion as et where we can present specific resolutions, but I hope before this eeting adjourns that we can all agree that it would be advisable, ighly advisable, that Congress should be asked to vest in some ranch of the Government the authority to investigate and to advise, least, regarding substances other than foods entering into interate commerce. I think we ought to be able to agree on that.

I have been assigned to open the discussion, and, as I said, I am oing to be brief. In fact, I do not catch points presented verally very readily; but there were three which I caught this morng which stick in my mind. They stand out like mountain peaks. ne of them was reported by Doctor Sayers. He reported that here was 10 per cent of lead in the dust of his experimental chamer. Exhaust gases had been going through there for some months. xhaust gases go through garages for a very much longer time an that. We may therefore take that observation as an indicaion of what the dust in a garage is going to consist of, namely, 0 per cent of lead.

Another point which struck me profoundly was that presented y Doctor Kehoe, that his controls were poisoned. I should not ave said poisoned, I should say his controls became leaded, and think he implied that this was due to the lead from the lead thyl which he had around there being in some manner released, etting loose, going into dust, or vapor, or in some way getting nto his control animals. That, I think, is a very fair illustration f what the sanitary experts expect with regard to conditions here you have a material of the high toxicity of tetraethyl lead, r of lead in any form lying about.

Then a third point, which I shall want to come back to, was made by Doctor Flinn, that tetraethyl lead, used even in small mounts, is absorbed through the skin, so that if you get it on your ands, it gets into the body in some way, either through the skin r through the respiratory tract. It is certainly a very striking act that even the experimenters, even the investigators, who cer-