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CHRONIC EXPOSURE OF CYNOMOLGUS MONKEYS
TO LEAD CHLOROBROMIDE SINGLY AND IN
BINARY COMBINATION WITH CERTAIN AIRBORNE
POLLUTANTS

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Hazleton Laboratories, Incorporated

Prepared for:

Coordinating Research Council, Incorporated

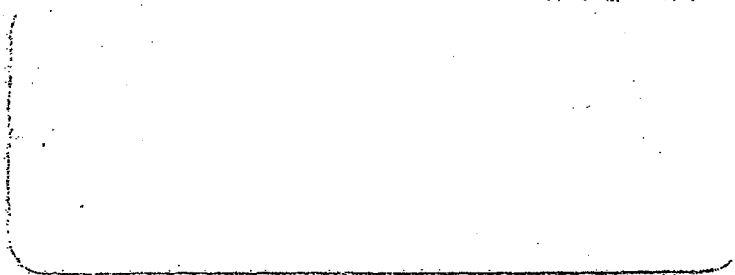
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BINARY COMBINATION WITH CERTAIN
AIRBORNE POLLUTANTS

Submitted to
Coordinating Research Council
Project CAPM-6-68

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a subsidiary of Environmental Sciences Corporation

SPONSOR: Coordinating Research Council (CAPM-6-68) DATE: April, 1972

MATERIAL: Lead Chlorobromide

SUBJECT: Study of Synergistic Effects of Certain Airborne Systems in the Primate: Chronic Exposure of Cynomolgus Monkeys to Lead Chlorobromide Singly and In Binary Combination with Certain Airborne Pollutants

I. INTRODUCTION

This study was initiated to determine the synergistic effects of five common air pollutants in cynomolgus monkeys (Macaca fascicularis) exposed continuously, 24 hours per day, seven days a week, for a period of 104 weeks. The pollutants examined, singly and in binary combination, were three gases, nitrogen dioxide, sulfur dioxide, and carbon monoxide and two particulates, calcium sulfate and lead chlorobromide. The nominal exposure levels selected and the current Threshold Limit Values (TLV) (1) presently set for each pollutant are presented in Table 1. The nominal particle size selected for the two particulates, calcium sulfate and lead chlorobromide, was less than two microns ($<2\mu$).

This report presents the results of measurements made on monkeys exposed to lead chlorobromide singly and in binary combination with nitrogen dioxide, sulfur dioxide, and carbon monoxide and briefly summarizes the methodology used. A series of technical reports have been issued describing the methodology in detail; these are listed in Table 2.



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Table 1 - Nominal exposure levels and current Threshold Limit Values.

<u>Agent</u>	<u>Nominal Concentration</u>	<u>TLV(1)</u>
Nitrogen dioxide	0.5 and 7.5 ppm	5 ppm
Sulfur dioxide	0.5 and 10.0 ppm	5 ppm
Carbon monoxide	20.0 and 67.5 ppm	50 ppm
Calcium sulfate	10.0 mg/m ³	"Inert" or Nuisance Particulate*
Lead chlorobromide	0.6 mg/m ³	0.15 mg/m ³ **

* A threshold limit of 10.0 mg/m³ is recommended for substances in this category and for which no specific threshold limit has been assigned.

** TLV for lead, (1971 intended change).



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Table 2 - Technical Reports

Report Number	Title	Status
1	Measurement of Total Respiratory Flow Resistance in Rodents	Submitted 12/66
2	Measurement of Pulmonary Flow Resistance, Dynamic Compliance, Tidal Volume, and Respiratory Rate in Normal and in Tracheotomized Rodents	Submitted 1/67
3	Measurement of Static Compliance in Tracheotomized Rodents	Submitted 1/67
4	Calibration Procedures for Airflow, Tidal Volume, and Pressure used in Measuring the Mechanical Properties of Rodent Lungs	Submitted 1/67
5	Technical Specifications of Equipment used in the Study of Rodent Mechanics	Submitted 1/67
6	Mechanics of Respiration in Cynomolgus Monkeys	Submitted 6/68
7	Calibration Procedures-Mechanics of Respiration in Cynomolgus Monkeys	Submitted 6/68
8	Specifications of Electronic Equipment-Mechanics of Respiration in Cynomolgus Monkeys	Submitted 6/68
9	Basic Documentation for the On-Line, Real-Time, Time Storing Computer System	In Preparation
10	Hazleton Laboratories' Multiplexer	Submitted 9/68
11	Measurement of Total Respiratory Flow Resistance in Primates	Submitted 9/68
12	Electrocardiograms on Monkeys	Submitted 9/68
13	Measurement of Distribution of Inspired Air in Cynomolgus Monkeys	Submitted 2/69
14	Pulmonary Diffusing Capacity in the Cynomolgus Monkey	Submitted 1/69



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Table 2 - Continued

<u>Report Number</u>	<u>Title</u>	<u>Status</u>
15	Lung Fixation Technique for Cynomolgus Monkeys	Submitted 9/68
16	Blood Gas Measurement System	Submitted 2/69
17	Carbon Monoxide Uptake in Rodents	Submitted 12/68
18	Exposure Chambers and Pollutant Systems	Submitted 9/69



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II. MATERIALS AND METHODS

1. ANIMALS, GROUPS, AND EXPOSURE DURATION

1.1. Animals

Young cynomolgus monkeys (Macaca fascicularis) obtained from Hartelust-Thorsen of Monmouth, New Jersey and weighing 1.6 - 3.0 kg were used in this study.

1.2. Animal Screening

Animals received in our laboratory were tested for tuberculosis, radiographed for pulmonary lesions, and observed for general health. They passed a screening procedure consisting of an evaluation of pulmonary function, ECG, hematology, and clinical chemistry. Animals having values within acceptable limits were assigned to this study.

1.3. Animal Groups

Seventy-two monkeys were randomized into eight groups; each group consisted of nine animals composed of five males and four females or vice versa. One group was maintained as the control group exposed to clean air while the seven other groups were exposed to the four pollutants, singly or in combination with another pollutant. Nominal concentrations and exposure duration are presented in Table 3 for each of the eight groups.



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Table 3 - Groups, nominal concentrations and exposure duration.

<u>Group</u>	<u>Nominal Concentration</u>	<u>Exposure Duration</u> weeks
1	Control	104
9	PbClBr - 0.6 mg/m ³	104
2	NO ₂ - 0.5 ppm	87
5	SO ₂ - 10.0 ppm	104
7	CO - 67.5 ppm	104
10	NO ₂ - 0.5 ppm PbClBr - 0.6 mg/m ³	104
18	SO ₂ - 10.0 ppm PbClBr - 0.6 mg/m ³	104
20	CO - 67.5 ppm PbClBr - 0.6 mg/m ³	104



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1.4. Pre-exposure Control and Exposure Duration

After placing the animals in the exposure chambers, a period of two weeks was allowed for adaptation during which time no measurements were made. A pre-exposure control period of eight weeks followed the two-week adaptation period when physiological variables were measured for each group of animals to establish control values and the weekly variation. Following the eight-week pre-exposure period, the 104-week exposure period was started. The exposure duration for the control group and six exposure groups was 104 weeks. The group exposed to 0.5 ppm NO₂, exposed for a period of 87 weeks, was a repeat group for a group that was accidentally overexposed during Week 22.

2. EXPOSURE CONDITIONS

2.1. Exposure Chamber

One of the exposure chambers used during the 104-week experiment with cynomolgus monkeys is shown in Figure 1. The chambers were fabricated from 304 L stainless steel with glass windows and were 6' x 6' x 5' with pyramidal tops and bottoms.

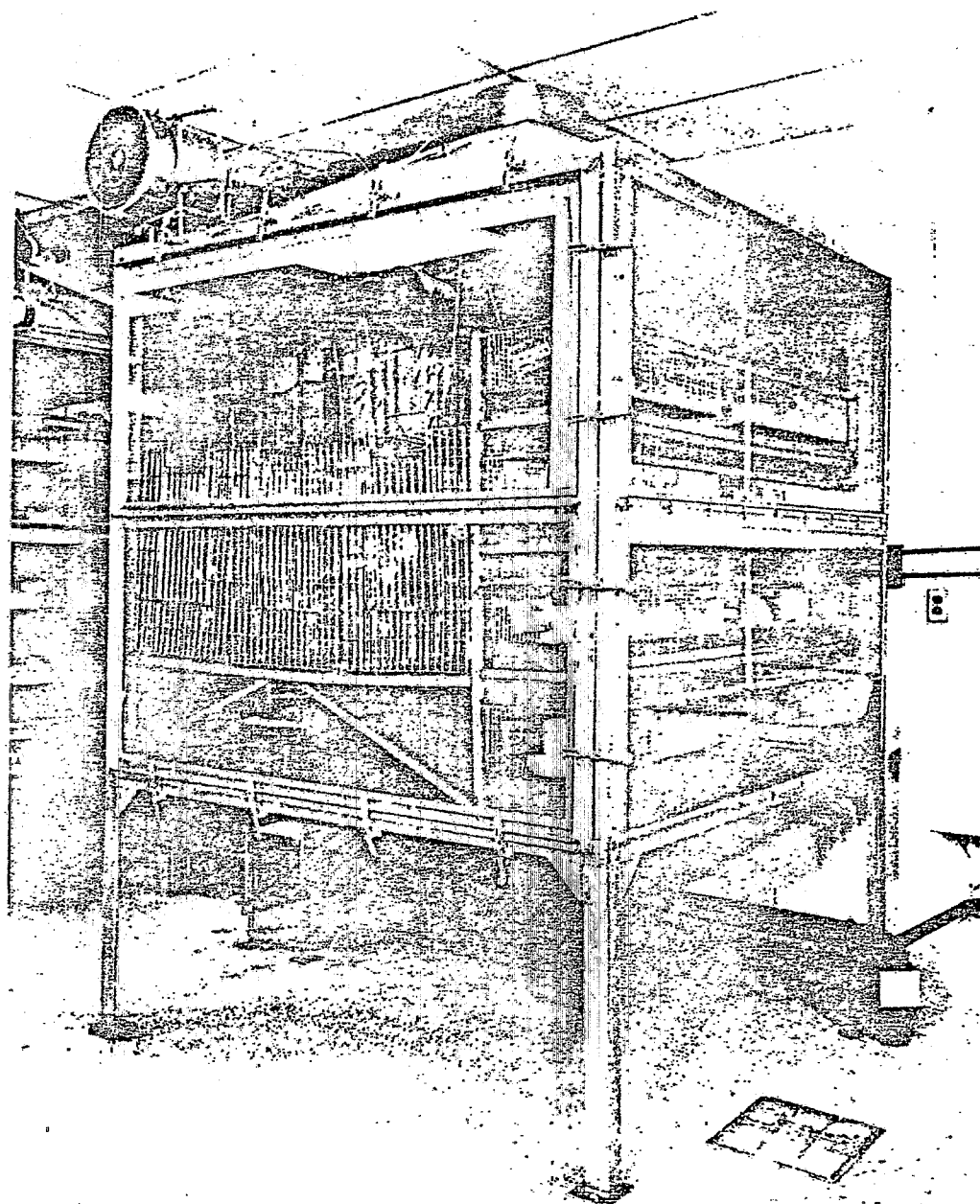


Figure 1 - Exposure chamber housing nine cynomolgus monkeys and 48 rats for exposure to air pollutants.



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2.2. Animals in Exposure Chamber

Each chamber was designed to house nine monkey cages each holding one animal. The cages were arranged in three rows of three cages all on the same tier as can be seen from the diagram presented in Figure 2. Each cage was made from stainless steel bars and was 16 1/2" wide, 24" high, and 21" long; a photograph is presented in Figure 3. The chamber also accommodates four tiers of stainless steel rat cages supported on a stainless steel rack with dropping pans under each tier; these are discussed in another report.

2.3. Air Supply to the Exposure Chamber

The air supplied to each exposure chamber passed through a MSA Ultra Aire[®] filter. The temperature was maintained at $72^{\circ} \text{F} \pm 2^{\circ}$, and the relative humidity was maintained at $50\% \pm 5\%$. The airflow through each chamber was slightly in excess of 1000 liters/minute.

3. METHODS OF GENERATION

3.1. Nitrogen Dioxide (NO_2)

Gas mixtures of 5% nitrogen dioxide in nitrogen were obtained from J. T. Baker Company. Known volumes of these gas mixtures were metered into the chamber air inlet and diluted with makeup air before entering the exposure chamber turret.

3.2. Sulfur Dioxide (SO_2)

Sulfur dioxide was generated in the same manner as NO_2 except that compressed gas mixtures of 1% and 5% SO_2 in nitrogen were used. Chamber

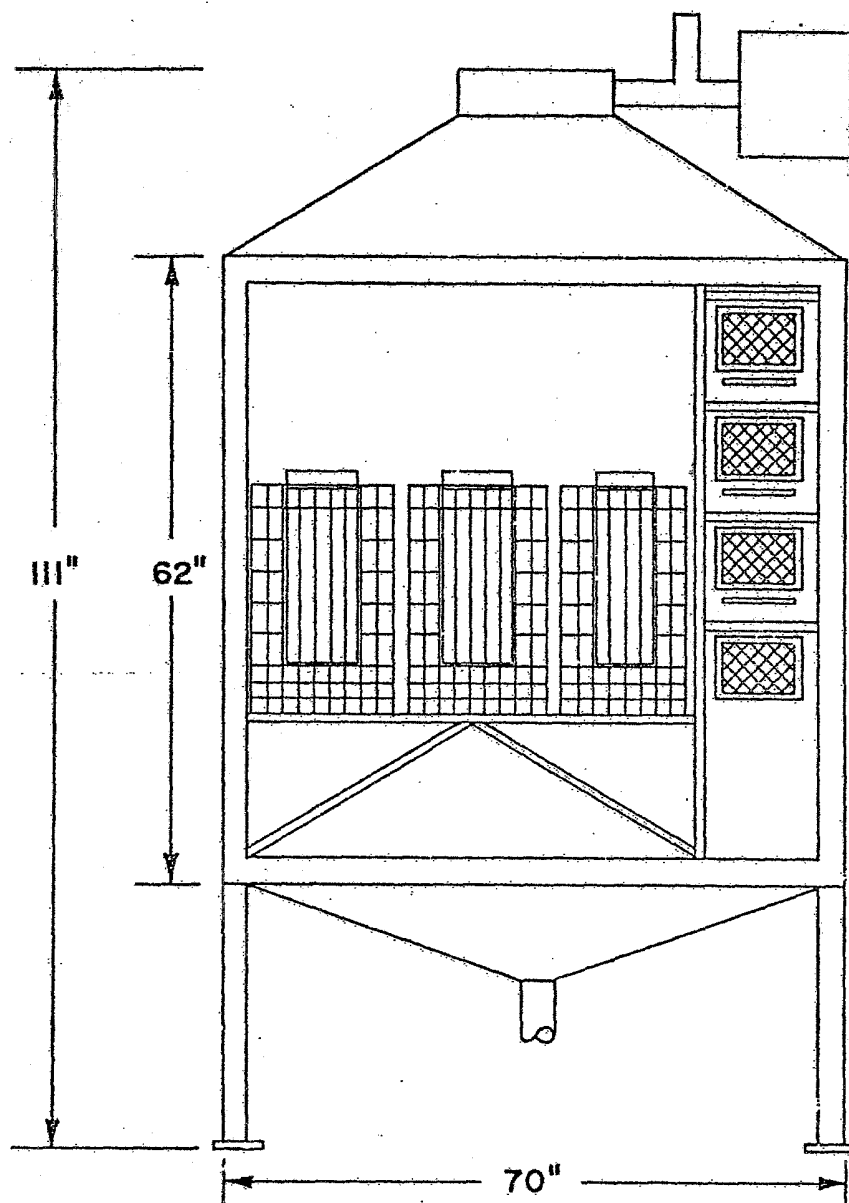


Figure 2 - Exposure chamber and distribution of cages for monkeys and rats.

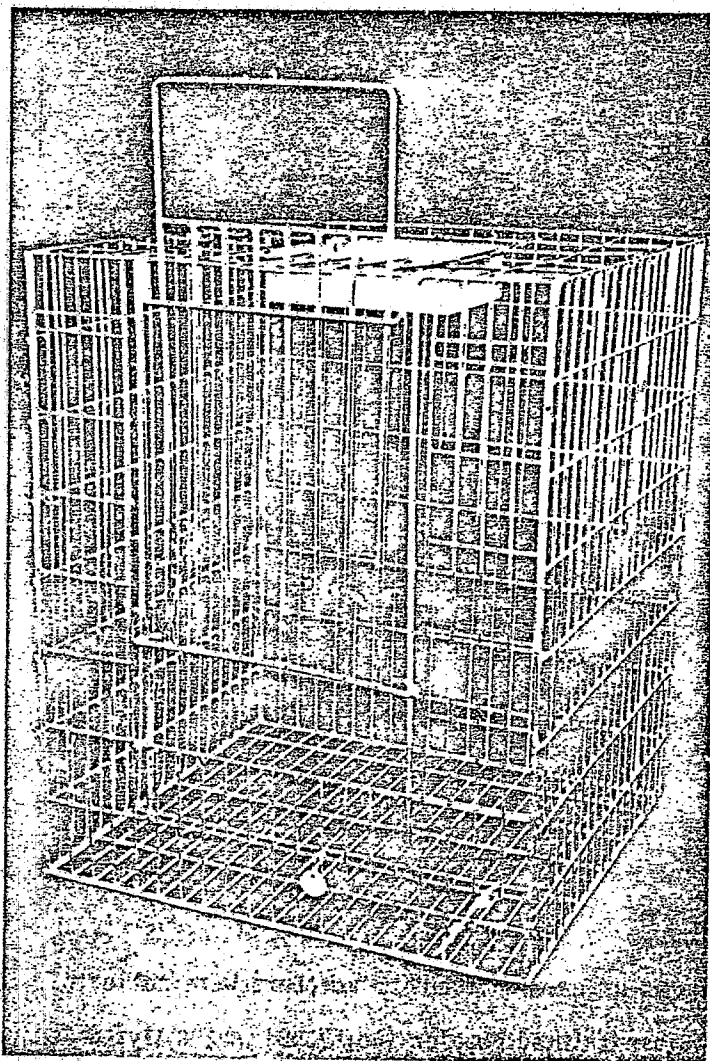


Figure 3 - Stainless steel cage for housing individual monkeys in exposure chambers.



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concentrations at 0.5 ppm SO_2 level were produced from 1% SO_2 mixtures, while chamber concentrations at the 10.0 ppm SO_2 level were produced from 5% SO_2 mixtures.

3.3. Carbon Monoxide (CO)

Carbon monoxide concentrations were generated by metering known volumes of pure (100%) CP Grade CO from compressed gas cylinders obtained from J. T. Baker Company and Air Products.

3.4. Lead Chlorobromide (PbClBr)

Lead chlorobromide was generated and introduced into the exposure chamber as airborne particulates by means of a Wright dust feed mechanism (Figure 4). The PbClBr was specially synthesized for this study by the Ethyl Corporation.

4. ANALYTICAL DETERMINATION OF CHAMBER CONCENTRATIONS

4.1. Nitrogen Dioxide

4.1.1. Wet Chemical Analysis

Samples of each chamber's atmosphere were collected with a standard Ace Glass-fritted bubbler (No. 7350) and analyzed according to the method reported by Saltzman (2), at least four times daily.

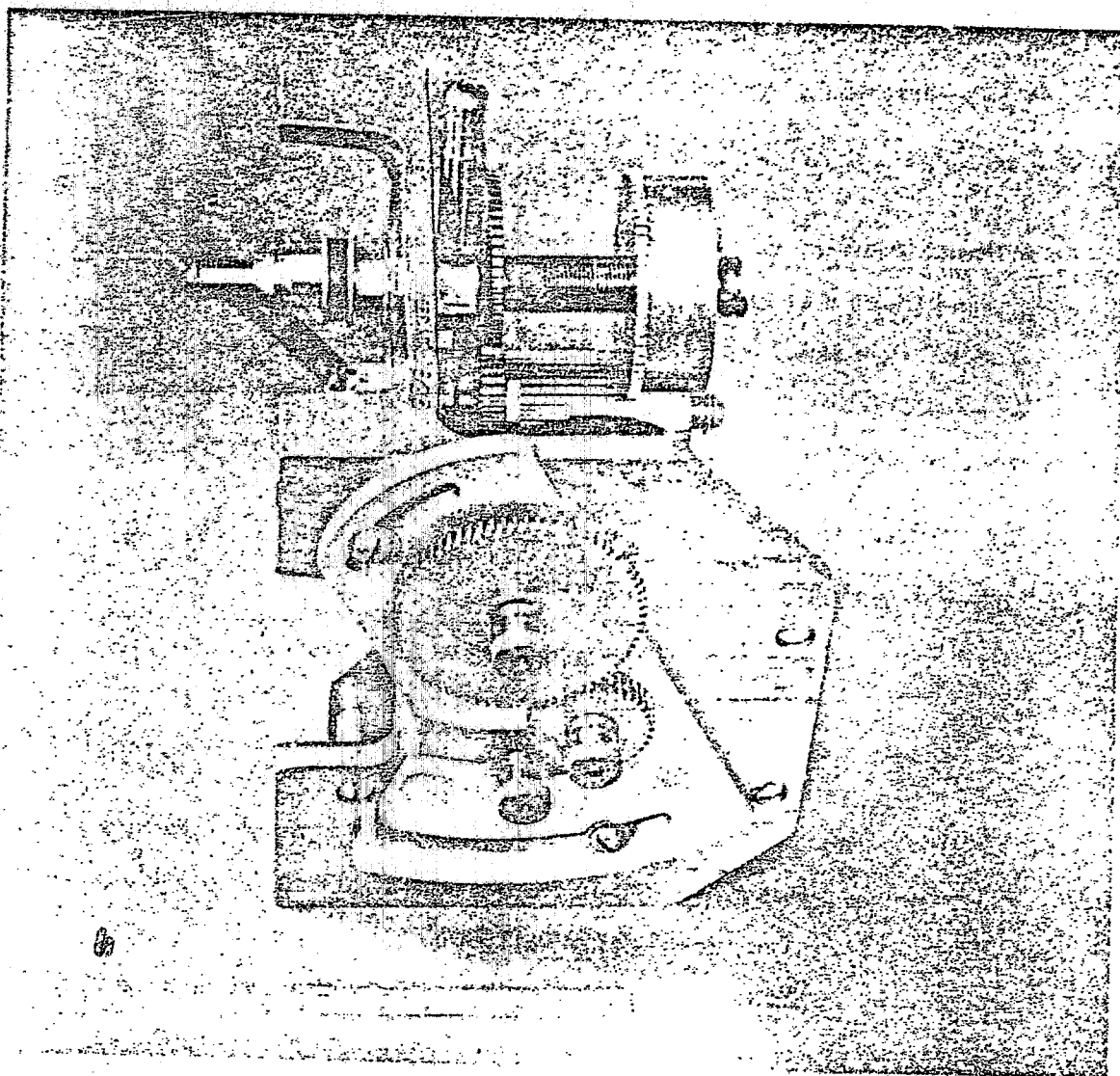


Figure 4 - Wright Dust Feed Mechanism.



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4.1.2. Instrumental Analysis

Instrumental analysis of chamber concentration of nitrogen dioxide was accomplished by using an Atlas Electric Devices Company NO_2 analyzer which was modified for our applications. The NO_2 analyzers were time-shared between a number of exposure chambers; thus, automatic samplers sequentially sampled a different chamber for six to 12 minutes out of each hour. The automatic samplers could be switched from automatic to a manual mode, and any single chamber could be monitored continuously.

4.2. Sulfur Dioxide

4.2.1. Wet Chemical Analysis

Samples of each chamber's atmosphere were taken once daily with an impinger and analyzed according to the method of West and Gaeke (3).

4.2.2. Instrumental Analysis

A Melpar Model SR-1100-1 sulfur dioxide analyzer (Figure 5) was used for continuous monitoring of chamber concentrations of sulfur dioxide and calibrated against the wet chemical method (3). The principal of operation was by photometric detection at the 394 $\text{m}\mu$ -centered band emitted by sulfur compounds in a hydrogen-rich air flame. The SO_2 analyzers were also used in conjunction with an automatic sequential sampler as described previously for NO_2 monitoring.

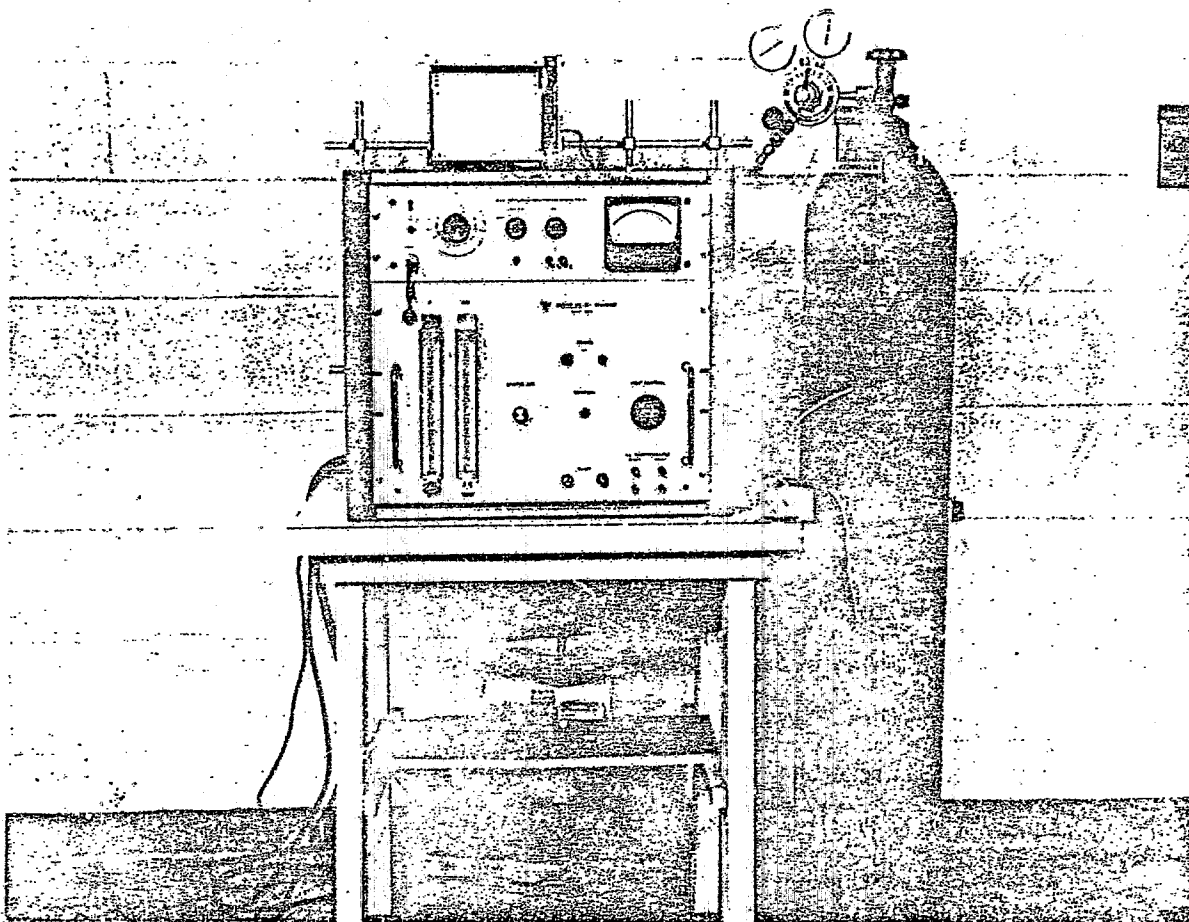


Figure 5 - Melpar sulfur dioxide analyzer.



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4.3. Carbon Monoxide

4.3.1. Instrumental Analysis

Analysis of animal exposure chamber atmospheres for carbon monoxide was accomplished by a dual-range, non-dispersive, infrared analyzer (Mine Safety Appliance Company, Lira Model 200). This instrument was used for chamber concentrations of 20 and 67.5 ppm CO. The analyzer was also operated in conjunction with an automatic sampler so that each chamber was monitored once each hour.

4.4. Lead Chlorobromide

4.4.1. Gravimetric Analysis

Samples of each chamber's atmosphere were collected once daily on membrane filters. The mass of lead chlorobromide was determined by weighing the filter before and after each exposure using a Cahn electrobalance. The concentration was then calculated based on net weight gain and the volume of air passed through the filter.

4.4.2. Wet Chemical Analysis

Wet chemical analysis for lead, using dithizone as reported by Fischer (4), was employed to confirm the results from the gravimetric analysis described above.

4.5. Particle Size Analysis

Particle size measurements of the PbClBr aerosols were performed using a Royco[®] Model 202 particle counter (Figure 6). The instrument was used to count and size airborne particles in 15 ranges from 0.15 to 6.0

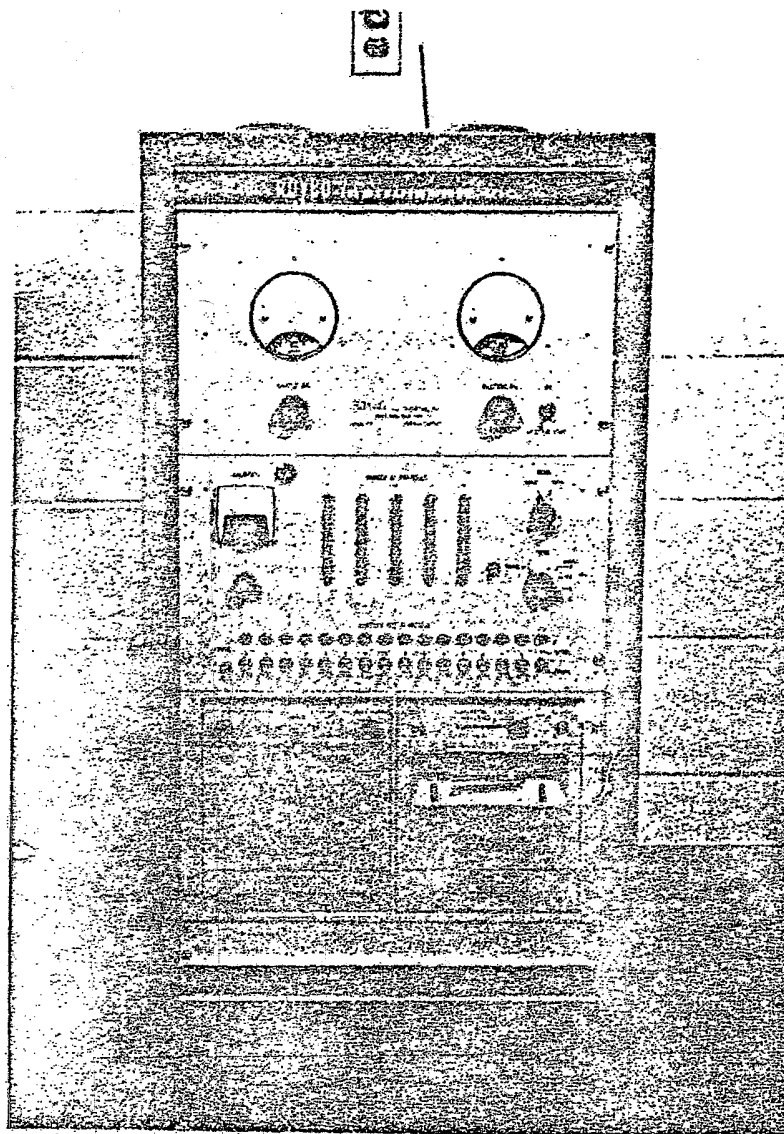


Figure 6 - Royco Model 202 particle size analyzer.



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microns. Count median diameter data was converted to mass median diameter by the conversion equations originally proposed by Hatch and Choate (5). To accomplish this conversion, the raw data from all samples taken from a given chamber were combined according to size intervals. From this pooled data a composite size vs. distribution graph was constructed on log-probability paper and the Hatch and Choate equations were applied.

5. BIOLOGICAL MEASUREMENTS

5.1. Body Weight and Clinical Signs

Body weights were tabulated six times during the pre-exposure control period and once a month during exposure until termination. The animals were observed daily for signs of toxicity and abnormal behavior.

5.2. Pulmonary Function Tests

Pulmonary function tests including measurements of the mechanical properties of the lung and respiratory system, distribution of ventilation, diffusing capacity of the lung, and arterial blood gas tension, were made on each animal periodically throughout the pre-exposure control period and the 104 weeks of exposure.

5.2.1. Mechanical Properties of the Lung

Several variables were measured to evaluate the mechanical properties of the lung. The measurements were made with the animal sitting in a chair or a body plethysmograph equipped with a face mask fitted to the monkey's nose and mouth. No anesthetic was used; however, a period of 10 to 15 minutes in the chair was needed to assure the measurements would be made when the monkey was relatively quite. Prior to the pre-exposure control period, all animals were acclimated



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to the test procedure. Figure 7 shows a picture of an animal sitting in the restraining chair, Figure 8 shows a picture of an animal sitting in a body plethysmograph, Figure 9 shows a close-up of the face mask placed on an animal, and Figure 10 shows the inside of the face mask used with the attached rubber dam. The inside of the mask was filled with epoxy resin to accomodate muzzle sizes of monkeys weighing from 1.2 to 6.0 kg., and thus providing a minimum amount of dead space. Four different sizes were used.

Two techniques were employed to evaluate the mechanical properties of the lung. The first method utilized a combination of techniques developed by Mead (6) and Murphy, et al. (7) and modified by Alarie et al. (8). This method involved subjecting the thorax of an animal to an oscillating pressure, sine wave in form, and at a frequency such that the mechanical reactance of the tissues was close to zero. Oscillating pressure around the thorax and airflow at the mouth were measured and the total respiratory system flow resistance during inspiration and expiration were separately calculated as the ratio of pressure to flow. Figure 11 shows an oscillograph tracing of applied pressure in the body plethysmograph and the resulting airflow measured at the face mask during normal breathing with the animal sitting quietly in a body plethysmograph.

The second method utilized a combination of techniques developed by Andur and Mead (9) and Mead and Whittenberger (10) and modified by Alarie et al. (11). In this method a number of variables

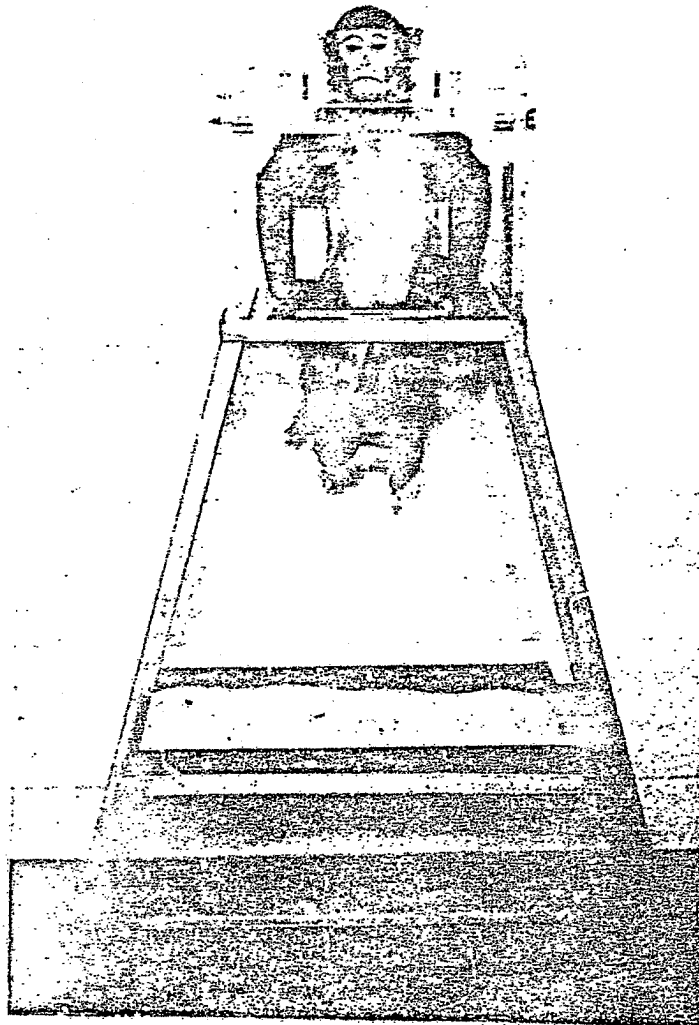


Figure 7 - Monkey seated in primate restraining chair.

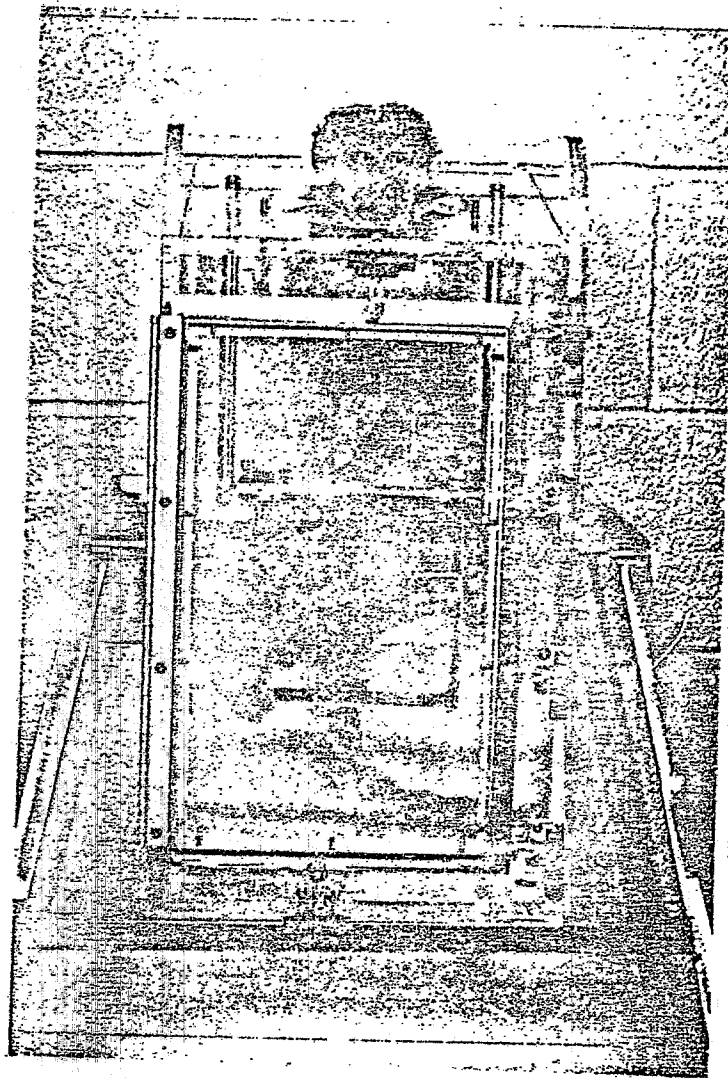


Figure 8 - View of the structure in the photograph.



Figure 9 - Front view of assembled face mask with open parts attached to primate chair with monkey's snout properly inserted. A rounded plate behind the head of the animal prevents him from withdrawing from the mask.

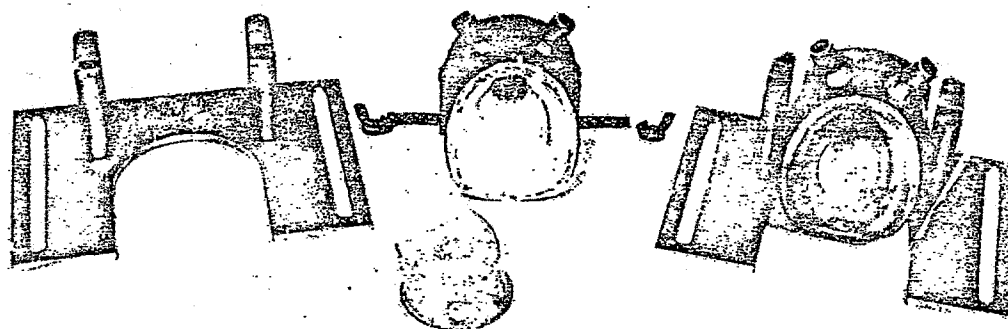


Figure 10 - Left - Base plate.

Center - Disassembled primate face mask with epoxy filling and the rubber dam.

Right - Assembled face mask with stretched rubber dam.

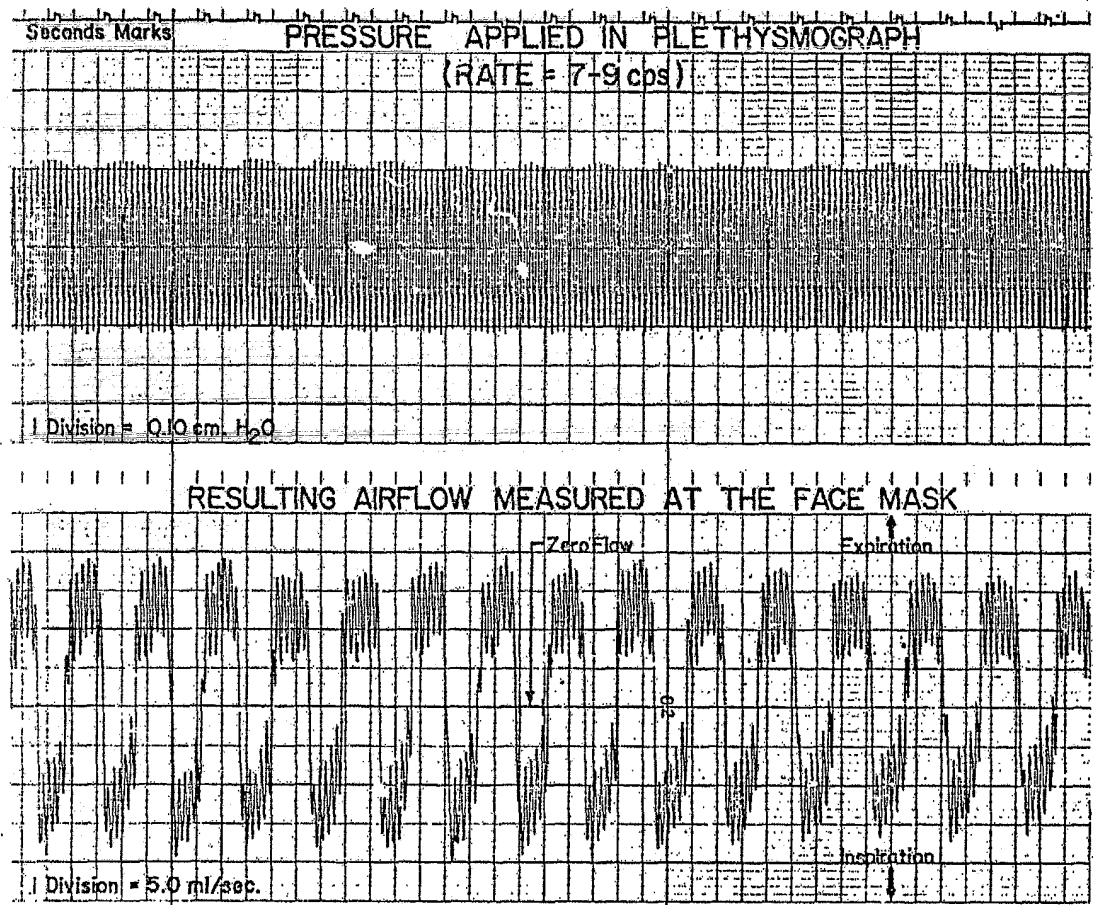


Figure 11 - Oscillograph tracing showing the applied pressure in the plethysmograph and the resulting airflow measured at the mask on a cynomolgus monkey sitting in the plethysmograph and breathing quietly.



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to evaluate the mechanical properties of the lung were calculated from direct measurement of airflow and of transpulmonary pressure via intra-pleural catheterization. Tidal volume was derived from integration of airflow during successive breathing cycles. Figure 12 shows an oscillographic tracing of tidal volume, airflow, and transpulmonary pressure. Further details on these techniques of measurement may be found in technical reports listed in Table 2.

The analogue signals recorded on the oscillograph were transmitted directly to an IBM 1800 computer system. The computerized techniques of data extraction were similar in principle to those described by Stacy and Peters (12), Peters and Stacy (13), and Dennis, et al. (14). Following the termination of each test, the results were printed in a typewriter located in the testing laboratory performing the test. The list of basic variables being measured and the frequency of measurement is presented in Table 4.

5.2.2. Distribution of Inspired Air and Ventilation

An open circuit technique described by Fowler (15, 16, 17) and modified by Alaire, et al. (18) was adapted for the measurement of nitrogen washout from the lung during pure oxygen breathing. Figure 13 presents a picture of an animal with a face mask and attachments needed to perform this test. Figure 14 shows the results obtained on the recording oscillograph. Further details on this technique can be found in the technical reports listed in Table 2. The list of basic variables being measured and the frequency of the measurement is presented in Table 5.

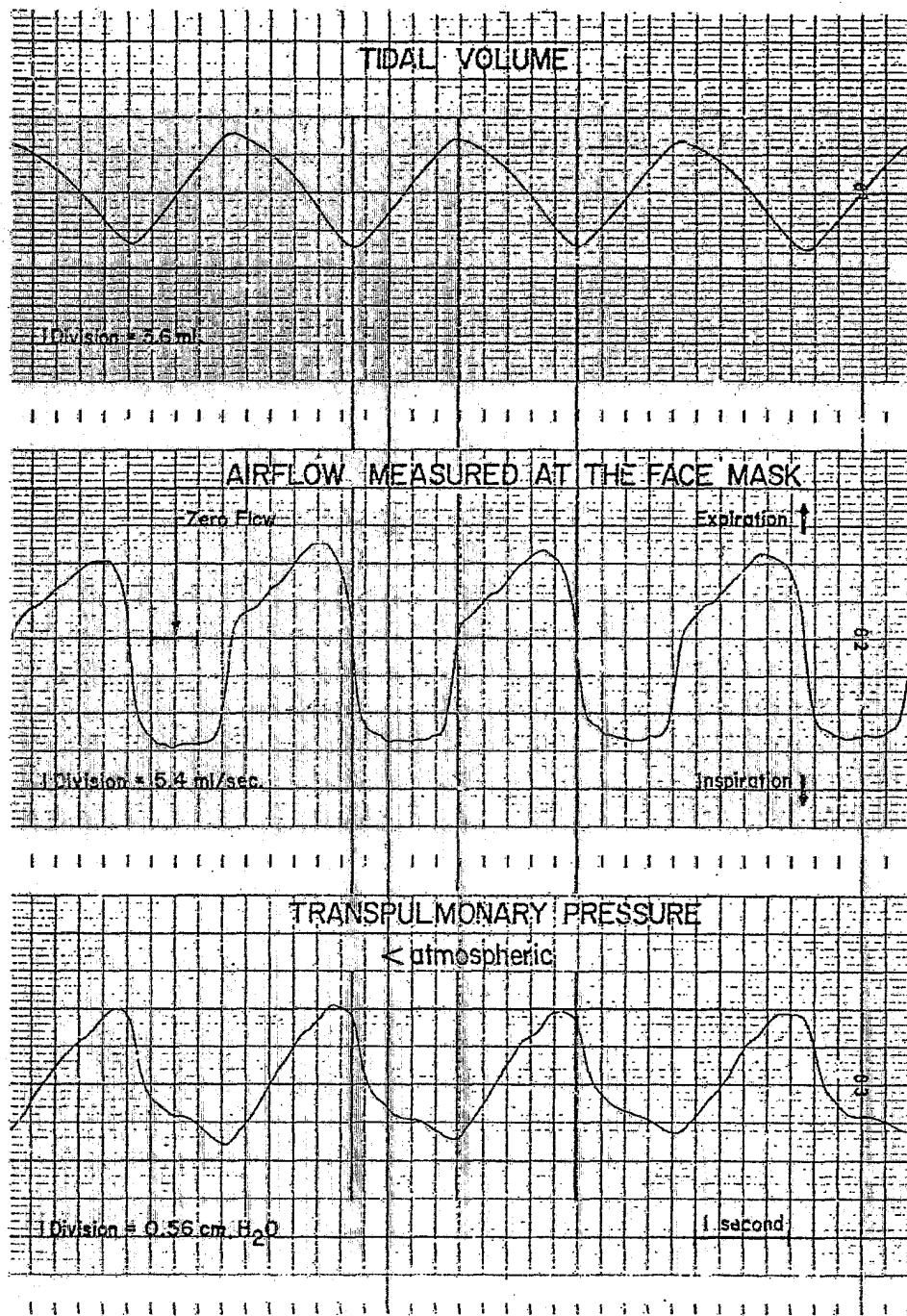


Figure 12 - Oscillograph tracing showing tidal volume, airflow at the mask, and transpulmonary pressure in a cynomolgus monkey sitting in a restraining chair and breathing quietly. Vertical lines drawn indicate simultaneous phases in the three measurements.



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Table 4 - Mechanical properties of the lung and respiratory system measured in cynomolgus monkeys during exposure for a period of 104 weeks.

<u>Variable</u>	<u>Abbreviation</u>	<u>Frequency of Measurement</u>
Total respiratory system flow resistance during inspiration	Rrs(i)	A
Total respiratory system flow resistance during expiration	Rrs(e)	A
Tidal Volume	V_T	B
Respiratory rate	RR	B
Dynamic compliance of the lung	Cdyn(l)	B
Pulmonary flow resistance	RI	B
Work of breathing during inspiration per ml tidal volume	$W(i)/ml V_T$	B
Work of breathing during expiration per ml tidal volume	$W(e)/ml V_T$	B

A - Measured on six occasions during the pre-exposure control period, every week during the first nine weeks of the exposure period, and every four weeks thereafter.

B - Measured on four occasions during the pre-exposure control period, every two weeks during the first 10 weeks of the exposure period, and every four weeks thereafter.

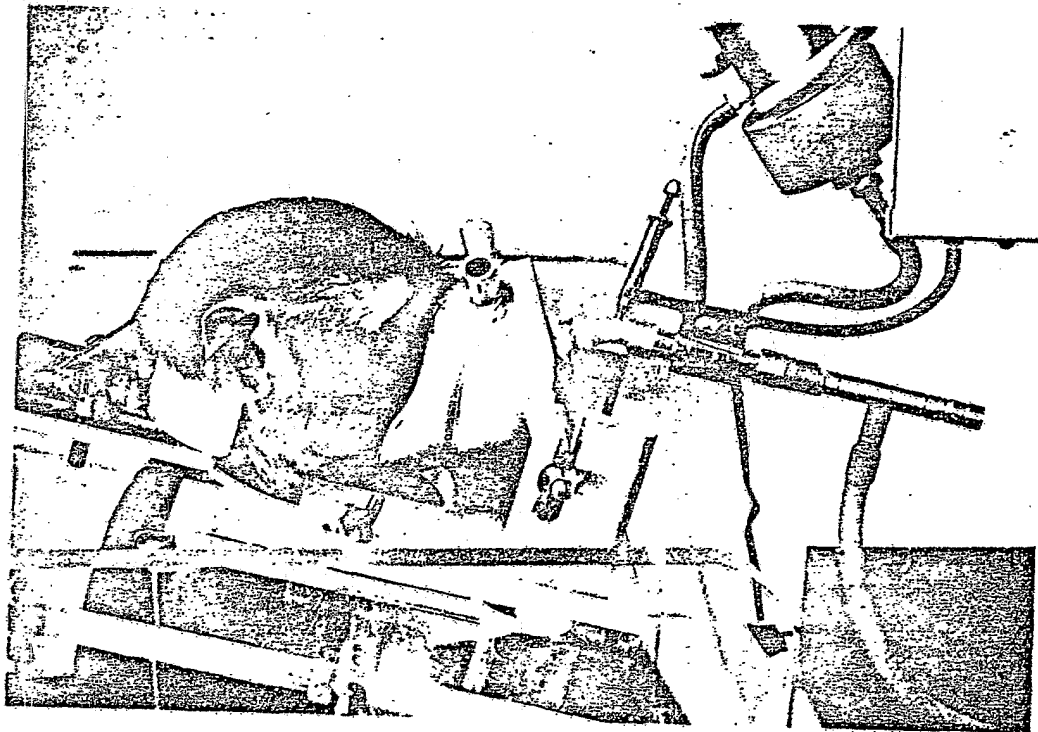


Figure 13 - Cynomolgus monkey in chair with face mask and needle valve for sampling nitrogen concentration and with attachment for change from air breathing to oxygen breathing.

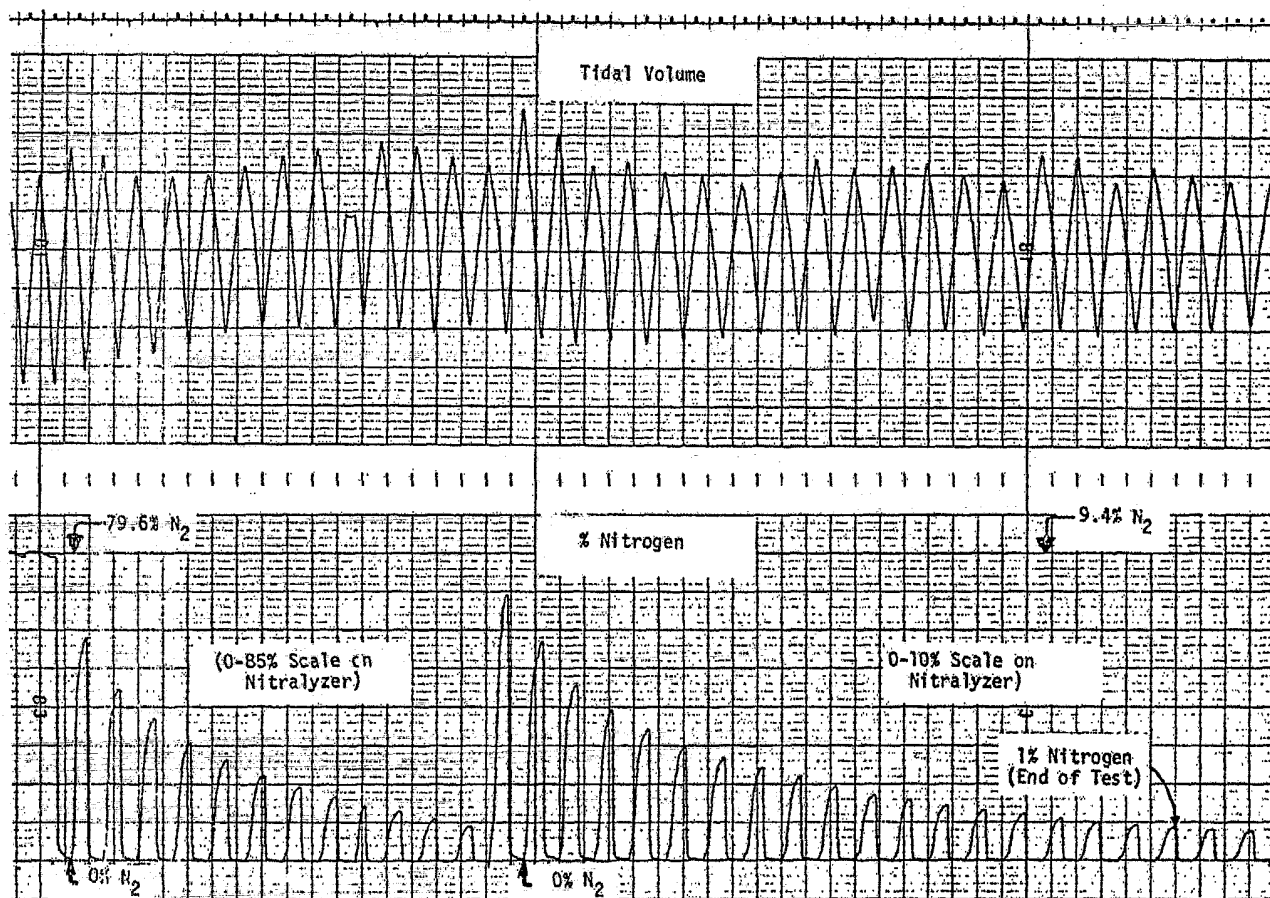


Figure 14 - Oscillograph tracing of tidal volume and % nitrogen during pure oxygen breathing showing nitrogen washout from the lung in cynomolgus monkeys.



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Table 5 - Ventilation and distribution of inspired air (nitrogen washout) measured in cynomolgus monkeys during exposure for a period of 104 weeks.

<u>Variable</u>	<u>Abbreviation</u>	<u>Frequency of Measurement</u>
Tidal volume	V_T	C
Respiratory rate	RR	C
Number of breaths to 1% nitrogen	$N(1\% N_2)$	C
Cumulative tidal volume to 1% nitrogen	$CV_T(1\% N_2)$	C

C - Measured on six occasions during the pre-exposure control period, every two weeks during the first four weeks of the exposure period, and every four weeks thereafter.



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5.2.3. Diffusing Capacity of the Lung

The carbon monoxide uptake and the diffusing capacity of the lung were measured by a rebreathing technique based on the same principles as those described by Bates (19), Lewis, et al. (20), Kruhoffer, et al. (21), and Long and Hatch (22) after modification for its use with monkeys. To perform this test, the animal breathes from a closed loop system containing 0.06% carbon monoxide. The decrease with time in carbon monoxide concentration, monitored continuously with an infrared analyzer, is used to calculate the animal's carbon monoxide uptake, which provides an index of an animal's diffusional properties. A picture of an animal connected to a rebreathing bag and closed circuit is presented in Figure 15. Further details on this technique can be found in the technical reports listed in Table 2. The basic variable measured and the frequency of measurement is listed in Table 6.

5.2.4. Arterial Blood Gas Analysis

Measurements on Arterial blood were performed using a Radiometer blood gas analyzer. A list of the variables measured and frequency of measurement is presented in Table 7. This measurement was performed 10-20 minutes after the intramuscular injection of phenylcyclidine (Sernylan[®]) for tranquilization of the animal. Blood was withdrawn from the femoral artery with the animal supine.

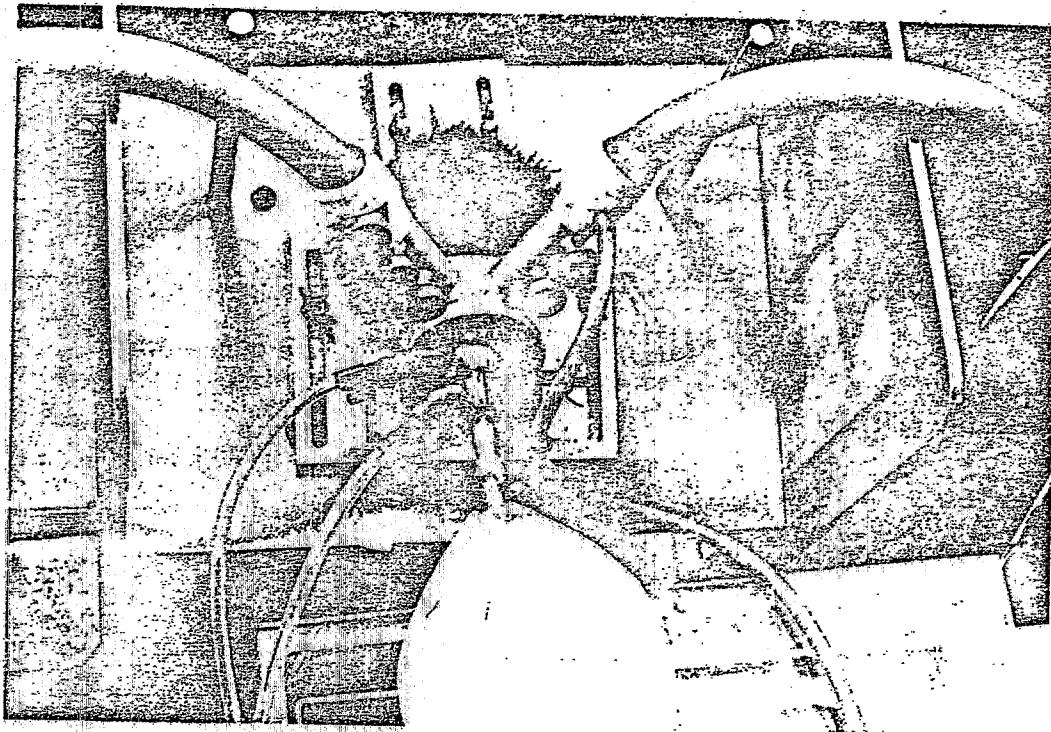


Figure 15 - Cynomolgus monkey with face mask, pneumotachograph, and rebreathing bag in place, and with the connection to a closed circuit for the measurement of carbon monoxide uptake in measuring $\dot{V}_{O_2}$



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Table 6 - Gas diffusion measurements in cynomolgus monkeys during exposure for a period of 104 weeks.

<u>Variable</u>	<u>Abbreviation</u>	<u>Frequency of Measurement</u>
Diffusing capacity of the lung for carbon monoxide	DL _{CO}	C

C - Measured on six occasions during the pre-exposure control period, every two weeks during the first four weeks of the exposure period, and every four weeks thereafter.

Table 7 - Arterial blood gas measurements in cynomolgus monkeys during exposure for a period of 104 weeks.

<u>Variable</u>	<u>Abbreviation</u>	<u>Frequency of Measurement</u>
Arterial blood oxygen tension	P _a O ₂	D
Arterial blood carbon dioxide tension	P _a CO ₂	D
Arterial blood acidity	pH	D
Plasma bicarbonate	plasma HCO ₃ ⁻	D

D - Measured once during the pre-exposure control period, at Weeks 1, 6, 13, during the exposure period, and every 13 weeks thereafter.



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5.3. Routine Hematology and Serum Biochemistry

Several hematological and serum biochemical determinations were made on all animals in the control group and the seven exposure groups. The blood was obtained from the femoral artery. The variables and the frequency of measurement are presented in Table 8.

5.5. Special Tests

5.4.1. Osmotic Fragility of Erythrocytes

Erythrocyte osmotic fragility studies were done during the last 24 weeks of exposure on the monkeys exposed to $PbCl_2$, NO_2 , and CO , alone and in combination, and the controls. These studies were done using a Kalmedic Fragilograph and the procedure described by Danon (23). This procedure simultaneously records fragility and salt concentration curves permitting an analysis of percent hemolysis of erythrocytes as a function of salt concentration. An evaluation of the 50% and 80% hemolysis levels were used to compare the effects of the various test compounds.

5.4.2. Carboxyhemoglobin

Carboxyhemoglobin (HbCO) levels were measured in the blood of monkeys from the control group and those exposed to 20.0 and 67.5 ppm CO , singly and in combination with the other pollutants. Measurements were made on one occasion prior to exposure, weekly during the first four exposure weeks and every 12 weeks thereafter using the procedure of Commins and Lawther (24).



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Table 8 - Hematological and serum biochemical determinations in cynomolgus monkeys performed during exposure for a period of 104 weeks.

Variable	Abbreviation	Frequency of Measurement
Hematocrit	Hct.	E
Hemoglobin	Hgb.	E
Total erythrocyte counts	RBC	E
Total leukocyte counts	WBC	E
Blood glucose	Glu.	E
Blood urea nitrogen	BUN	E
Total serum bilirubin	-	E
Total serum protein	-	E
Serum albumin	-	E
Serum sodium	Na	E
Serum potassium	K	E
Serum chlorides	Cl	E
Serum calcium	Ca	E
Serum carbon dioxide	CO ₂	E
Serum glutamic-oxaloacetic transaminase	SGOT	E
Serum glutamic-pyruvic transaminase	SGPT	E
Serum lactic acid dehydrogenase	LDH	E
Serum alkaline phosphatase	Alk. PO ₄	E

E - Measured once during the pre-exposure control period and at 4, 16, 40, 68, and 104 weeks postexposure.



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5.4.3. Blood Lead

Analysis for blood lead levels were performed by atomic absorption spectrophotometry (25). Measurements were made in the monkeys from the control group and from the groups exposed to 0.6 mg/m^3 PbClBr , singly and in combination with NO_2 , SO_2 , and CO two times prior to exposure, weekly during the first 10 weeks of exposure, and every 12 weeks thereafter until termination of the exposure period.

5.4.4. Delta-Aminolevulinic Acid

Analyses of delta-aminolevulinic acid (δ -ALA) in the urine were made by the chromatographic procedure described by Marver, et. al. (26). Measurements were made on the animals from the control group and the groups exposed to 0.6 mg/m^3 PbClBr singly and in combination with NO_2 , SO_2 , and CO , once prior to exposure and at Weeks 1, 4, 16, 40, 68, and 104 during the exposure period.

5.4.5. Urinary Coproporphyrins

Urinary coproporphyrin determinations were made on the animals from the control group and those exposed to PbClBr singly and in combination with NO_2 , SO_2 , and CO . The frequency of measurement was the same as for δ -ALA described above. Analyses of urinary coproporphyrin levels were performed using standard fluorometric techniques (27, 28).



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5.5. Pathology

5.5.1. Gross Examination

Following 104 weeks of exposure, all surviving animals were sacrificed and necropsied. Animals which died during the 104 weeks were necropsied immediately. At necropsy, the lungs were removed, inflated, and perfused intratracheally with a volume of 10% neutral buffered formalin equal to the tidal volume for that particular animal. In addition, the following organs were removed and fixed in 10% neutral buffered formalin: brain, pituitary, thyroid, heart, thoracic aorta, liver, gall bladder, spleen, kidneys, adrenals, stomach, pancreas, duodenum, colon, peri-bronchial lymph nodes, urinary bladder, gonads, rib end, sternum, skeletal muscle, peripheral nerve, abdominal aorta, mesenteric lymph node, knee joint, and femur. Each animal was examined thoroughly for gross lesions and any abnormalities were recorded.

5.5.2. Organ Weights

From each animal the following organ weights were recorded: brain, thyroid, lungs, heart, liver, kidneys, and adrenals. These were used to calculate organ/body weight ratios.

5.5.3. Microscopic Examination

The following tissues were dehydrated in graded alcohol, infiltrated and embedded in Paraplast, sectioned at five microns, and stained with hematoxylin and eosin: trachea, lung (each of the seven



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lobes), heart, liver, kidney, and peribronchial lymph node. These sections were examined by a pathologist who described in detail any microscopic changes and summarized these findings for each group.

6. STATISTICAL METHODS

6.1. Introduction

This experiment was designed to study the biological effects on cynomolgus monkeys resulting from 24 months of exposure to various air pollutants. These pollutants were administered singly and in binary combinations with each other. A control group was also employed which was exposed under the same conditions to filtered air. Each group initially contained nine (9) monkeys consisting of five males and four females or vice versa.

The biological measurements made on these animals consisted of both pulmonary physiology variables and blood variables (i.e., serum chemistry and hematology). These measurements were made several times prior to the start of exposure, typically six (bi-weekly) measurements for the physiology and one measurement for blood variables, to establish an initial base-line for each animal group. After the exposure started, the biological measurements were made at approximately the same frequency as pre-exposure for the first six months after which the measurements were made less frequently. The rationale for the differential frequency



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of measurements was the desire to detect any early gross compound effect as soon as possible. It was expected that any changes which occurred after this initial exposure phase would be gradual changes; therefore, the measurement frequency could appropriately be decreased.

Eight experimental groups (Table 3) relevant to the evaluation of $PbClBr$ effects were arranged into four statistical groupings (Table 9) for analytical purposes. Within the constraints of the experimental design, these four statistical groups provide all relevant comparisons relating to $PbClBr$. The first statistical grouping is comprised of the control group and one group exposed to $PbClBr$ alone. The remaining three statistical groupings are each comprised of the following: a binary combination group containing $PbClBr$ and one other pollutant such as NO_2 , SO_2 , or CO ; the control group; and the two single pollutant groups, exposed to the same respective concentrations as the binary group.

6.2. Evaluation of Treatment Effects

6.2.1. Regression Analyses

The male and female values were combined for body weight and all pulmonary function variables. These parameters were first analyzed by an analysis of variance of regression. The mean pre-exposure value of each animal was used as his initial base-line response just prior to start of exposure; each animal's individual values were used at each



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Table 9 - Statistical groupings for the determination of synergistic effects between lead chlorobromide and certain other pollutants.

<u>Group</u>	<u>Pollutant</u>	<u>Nominal Concentration</u>
A	Control Pb	- 0.6 mg/m ³
B	Control NO ₂ Pb ₂ NO ₂ + Pb ₂ +	- 0.5 ppm ³ 0.6 mg/m ³ 0.5 ppm ³ 0.6 mg/m ³
C	Control SO ₂ Pb ₂ SO ₂ + Pb ₂ +	- 10.0 ppm ³ 0.6 mg/m ³ 10.0 ppm ³ 0.6 mg/m ³
D	Control CO Pb CO + Pb	- 67.5 ppm ³ 0.6 mg/m ³ 67.5 ppm ³ 0.6 mg/m ³



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interval thereafter. This analysis tested for non-parallelism between the time-related response patterns of the various groups. This analysis, using repeated measures of individual animals, resulted in over-estimation of the degrees of freedom, due to the correlation between successive responses. While this may have resulted in an over estimation of the true frequency of differences, for a first analysis, this approach was desirable to ensure that all possible significant effects would be evaluated in more detail by other statistical methods.

A third degree polynomial regression curve was fitted to the interval means (29, 30, 31) to compare individual groups for possible mean differences. This procedure used the means at each interval (in contrast to the above analysis) thereby accounting for the correlation between an individual's response. Inspection of these plots within a statistical grouping allowed a judgment to be made as to the need for additional statistical analysis for group differences; especially when the data indicated abrupt changes in the mean level of one or more groups.

6.2.2. CUSUM Technique

In some instances, a cumulative sum (CUSUM) technique (32, 33, 34) was used to establish the time of occurrence of a sudden change in the mean level for a group. This CUSUM technique was extended to detect a change in differences between mean levels of the control group and any of the exposed groups by forming a time-paired difference between



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the individual cumulative sums. When such changes were detected, the means of the time segments after the change were compared by a t-test of the pre-exposure-adjusted means.

6.2.3. t-tests

In certain cases where pre-exposure differences were observed in a given parameter and whether or not group differences were found during exposure (e.g., differences in the CUSUM exposure-period means) between two or more groups, separate t-tests were made on these exposure segments. The pre-exposure mean for each animal was used to adjust its exposure period measurements by subtracting each animal's pre-exposure mean from each of its exposure values. The mean of these residuals for each animal was used to derive a new group mean for each group. The difference between these group means was then subjected to the t-test, with $n+m-2$ degrees of freedom (except when heterogeneous variances required adjustment of the degrees of freedom).

6.2.4. Analysis of Variance

The hematology and clinical chemistry data were analyzed by a factorial analysis of variance (35) for those statistical groups which constituted a factorial arrangement. Tests for compound effects and interactions between compounds were performed. Due to the transient nature of the changes generally found in these variables, this analysis was done at each interval rather than with time as an added factor in an expanded factorial design.

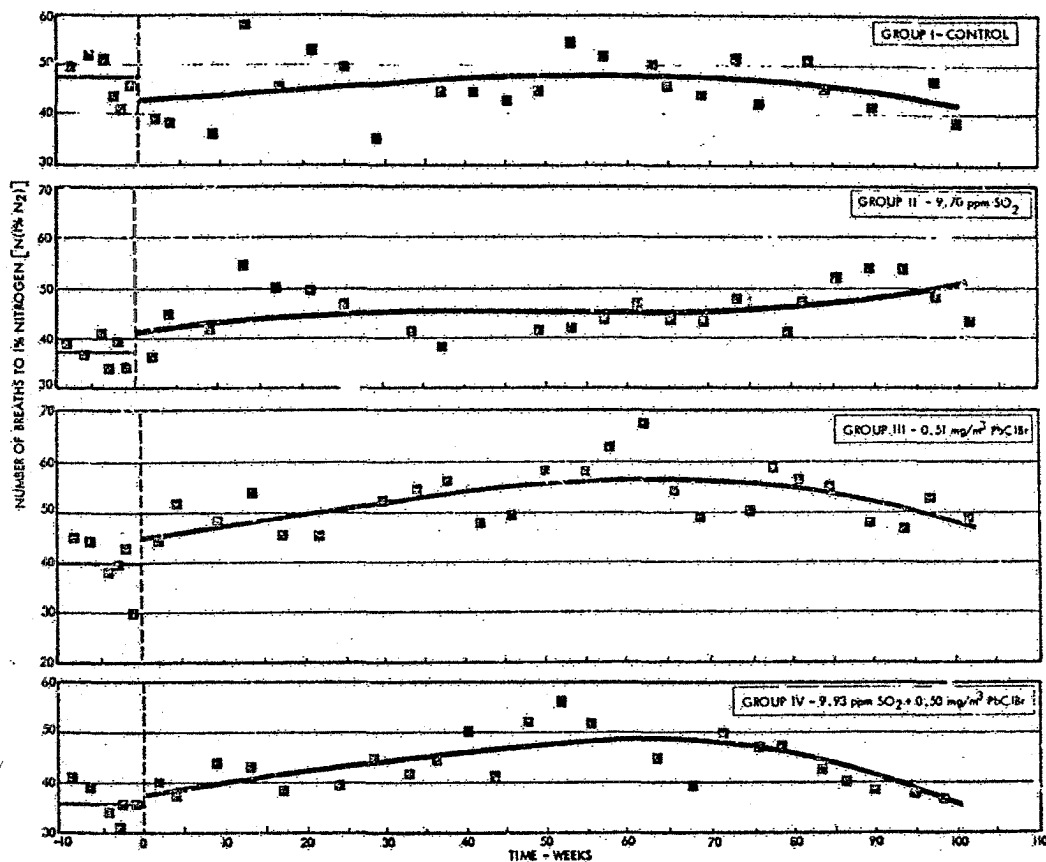


Figure 62 - Third degree polynomial regression curves for N(1% N₂) prior to and during exposure to sulfur dioxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.



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3.3.3.2. Respiratory Rate Measured During Pure Oxygen Breathing (RR')

Analysis of variance of regression for RR' (Table 15, Appendix C) indicated no significant slope differences among the groups. The third degree polynomial regression curves are presented in Figure 63. Inspection of Figure 63 indicated that RR' values for Groups I and II were essentially the same during the pre-exposure period and the entire exposure period. However, RR' values for Groups III and IV were higher than Group I following the forty-fifth week of exposure, and remained higher until the end of the experiment. Separate t-tests of the pre-exposure adjusted overall exposure means indicated that both Groups III and IV were significantly higher than Group I ($t = 2.61$, d.f. = 16 and $t = 2.28$, d.f. = 16, respectively).

3.3.3.3. Cumulative Tidal Volume from 80% to 1% Nitrogen [$CV_T(1\% N_2)$]

Analysis of variance of regression for $CV_T(1\% N_2)$ (Table 16, Appendix C) indicated no significant slope differences among the groups. The third degree polynomial regression curves are presented in Figure 64. Inspection of Figure 64 indicated that Group IV had somewhat lower CV_T values during the pre-exposure period and generally remained lower than the CV_T values for the other three groups during the exposure period. Values for Group III were slightly higher overall than Group I throughout the exposure period. A t-test of the pre-exposure adjusted overall exposure means comparing Groups I and III indicated that Group III was significantly higher ($t = 2.24$, d.f. = 13.7) throughout the exposure period.

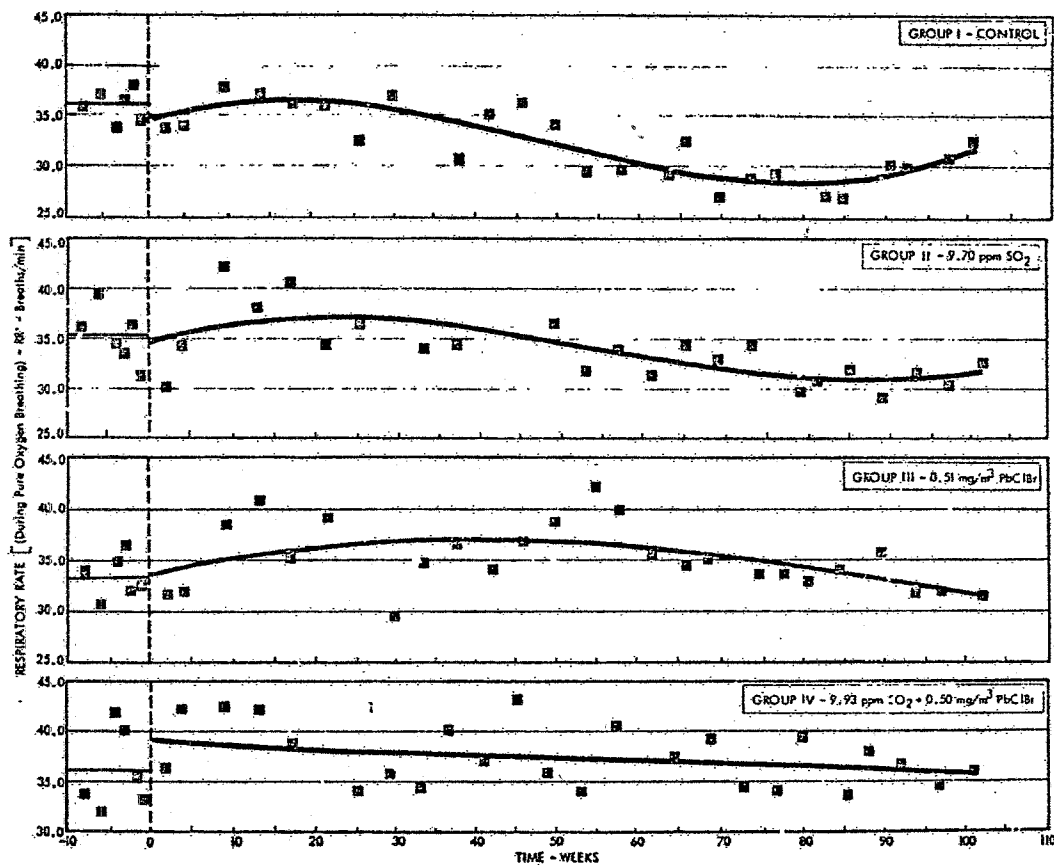


Figure 63 - Third degree polynomial regression curves for RR' prior to and during exposure to sulfur dioxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.

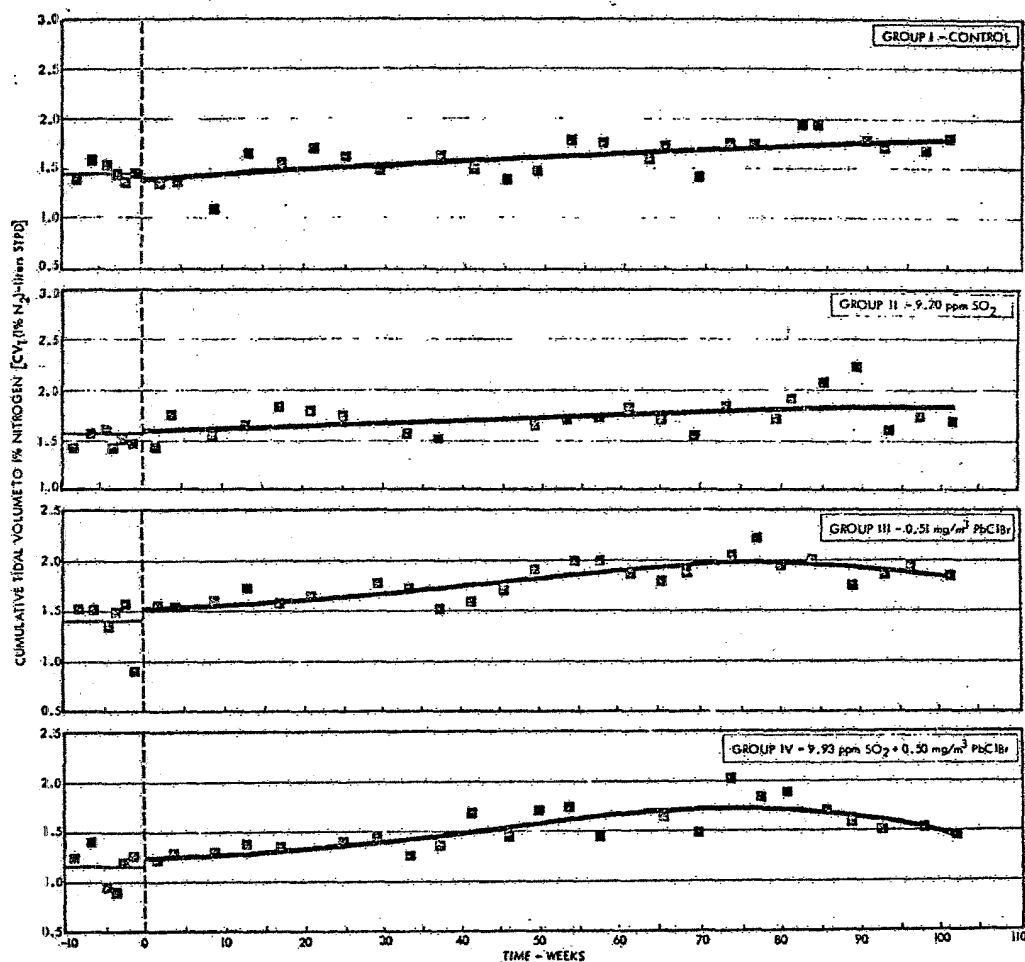


Figure 64 - Third degree polynomial regression curves for CVT(1% N₂) prior to and during exposure to sulfur dioxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.



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3.3.3.4. Tidal Volume Measured During Pure Oxygen Breathing (V_T')

Analysis of variance of regression for V_T' (Table 17, Appendix C) revealed non-parallelism among the groups. The third degree polynomial regression curves are presented in Figure 65. Inspection of Figure 65 indicated that Groups I, III, and IV increased slightly with time while Group II maintained a constant level throughout the experiment. A t-test of the pre-exposure adjusted overall exposure means indicated that Group II was significantly lower than Group I ($t = 2.44$, d.f. = 16) throughout the exposure period.

3.4. Hematology

The group means and analysis of variances of the various hematological variables measured are presented in Tables 18, 19, 20, and 21, Appendix C. No consistent trends were noted in any of these variables which remained within normal limits throughout. Random statistically significant differences were seen, but were not consistently related to the exposure conditions.

3.5. Clinical Biochemistry

The group means, standard errors, and the results of the analysis of variance of the various clinical biochemical variables measured are presented in Tables 22 through 35, Appendix C. Scattered statistically significant differences were noted; however, no trends were seen in any of the variables. Throughout the study, the group mean values fluctuated within the normal ranges of these variables.

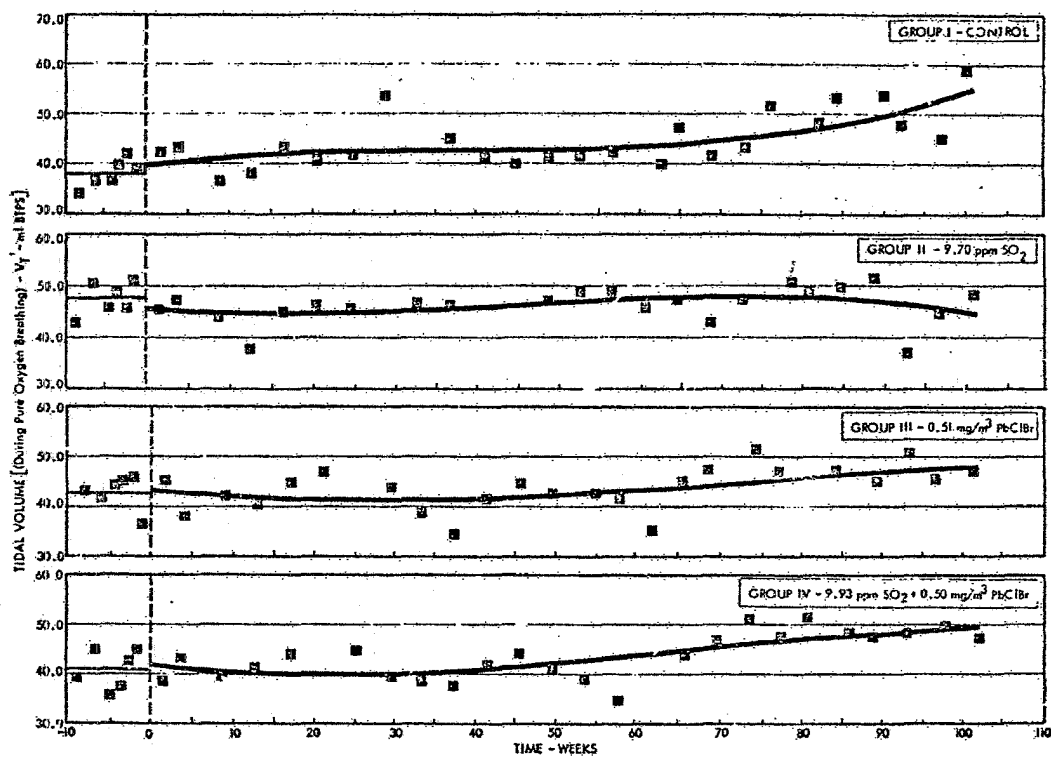


Figure 65 - Third degree polynomial regression curves for V_T' prior to and during exposure to sulfur dioxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.



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3.6. Arterial Blood Gas and pH

The group means and standard errors for the blood gas variables are presented in Table 36, Appendix C. Examination of these data did not reveal any consistent trend with time. No apparent exposure-related changes were seen in any of these variables.

3.7. Terminal Body Weight, Organ Weight, and Organ Weight as a Percentage of Body Weight

The data of the terminal body weight, organ weight, and organ/body weight ratios are presented in Tables 37 and 38, Appendix C for males and females, respectively. Several significant differences were found between the experimental groups and the control group. The adrenal weight for the males in Group II was significantly higher than Group I, and the adrenal weight and adrenal weight/body weight ratios for Group IV males were higher than Group I. The liver weight/body weight ratio for Group IV females was significantly higher than for Group I females. Several other significant differences were found from comparisons made between the various experimental groups; however, no consistent trends could be discerned.

3.8. Histopathology Summary

A detailed listing of the microscopic alterations seen in the lungs, tracheas, livers, kidneys, peribronchial lymph nodes, and hearts from the animals in the control and exposure groups are found in Table 39, Appendix C. Microscopic examination of the tissues from the animals exposed to $0.6 \text{ mg/m}^3 \text{ PbCl}_2$ and to the combination of $0.6 \text{ mg/m}^3 \text{ PbCl}_2$ and 10.0 ppm SO_2 revealed exposure-related alterations in the kidneys. These microscopic alterations were characterized by varying degrees of degeneration in the



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proximal convoluted tubules. The epithelial cells of the proximal convoluted tubules were vacuolated and possessed vesiculated nuclei. Numerous intranuclear, acid fast inclusion bodies were seen in the epithelial cells of the proximal convoluted tubules.

No other exposure-related microscopic alterations were seen in the lungs, liver, trachea, peribronchial lymph node or hearts. Scattered incidental lesions were seen in these organs from both the control and test animals. No difference in the incidence and severity of these lesions was seen when the controls were compared with the exposed groups.

Animal number 182L in the group exposed to 10.0 ppm SO_2 died during the 40th week of exposure. Microscopic examination of the tissues from this animal revealed lesions consistent of monkey pox in the lungs, liver, and trachea.

3.5. Summary

The inhalation exposure of male and female cynomolgus monkeys to 9.70 ppm SO_2 , 0.51 mg/m^3 PbClBr , and the combination of 9.93 ppm SO_2 plus 0.50 mg/m^3 PbClBr resulted in a deterioration in the distribution of ventilation in the animals in the two groups containing PbClBr . The number of breaths to 1% nitrogen and respiratory rate measured during pure oxygen breathing for both groups were significantly elevated above the controls, with respect to their relative pre-exposure values throughout the exposure period. Cumulative tidal volume to 1% nitrogen was significantly elevated in the group exposed to PbClBr alone, but this change was not seen in the



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group exposed to the combination of SO_2 and PbClBr . With the exception of higher breath to 1% nitrogen values than the control group, none of these differences were observed in the group exposed to 9.70 ppm SO_2 . This one difference was probably due to the high pre-exposure values of the control group.

Microscopic alterations related to the exposure to PbClBr were found in the kidneys of the animals of these two groups. These histopathological changes were characterized by varying degrees of degeneration of the proximal convoluted tubules. The epithelial cells of these tubules were vacuolated and possessed vesiculated nuclei. Numerous intranuclear, acid fast inclusion bodies were seen in these epithelial cells.

Body weight measurements made on both the control and exposed animals throughout the exposure period indicated that the animals in all groups increased in body weights. Analysis of these data did not reveal any significant differences in the rate of growth between the control and exposed animals. No meaningful differences were detected in terminal body weights, organ weights, or organ/body weight ratios between the control and exposed groups.

Hematological, clinical biochemical, and arterial blood gas measurements were made on both the control and exposed animals pre-exposure and periodically throughout the exposure period. No trends were detected in any of these variables in the exposed animals. No meaningful differences were detected between the control and exposed animals.



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Appendix C - Data compilations and summary of statistical analysis for

Statistical Grouping C, comprised of the following:

Group I - Control, Group II - 9.70 ppm SO₂, Group III -
0.51 mg/m³ PbClBr, and Group IV - 9.93 ppm SO₂ +
0.50 mg/m³ PbClBr.

Table 1 - Monthly means and the grand mean for the analytical concentrations of sulfur dioxide for Group II.

<u>Date</u>	<u>n</u>	<u>$\bar{x}$</u> ppm	<u>S.D.</u>
3/31/68 - 4/30/68	31	8.2971	1.8973
5/ 1/68 - 5/31/68	31	8.6948	2.1871
6/ 1/68 - 6/30/68	30	9.2770	1.4754
7/ 1/68 - 7/31/68	31	9.5377	1.1408
8/ 1/68 - 8/31/68	31	7.8032	2.2194
9/ 1/68 - 9/30/68	30	9.4020	1.6718
10/ 1/68 - 10/31/68	31	9.7019	1.9957
11/ 1/68 - 11/30/68	30	10.3617	0.9926
12/ 1/68 - 12/31/68	31	9.6352	1.1671
1/ 1/69 - 1/31/69	31	8.0226	2.1781
2/ 1/69 - 2/28/69	28	9.8011	0.7511
3/ 1/69 - 3/31/69	31	9.5323	1.3048
4/ 1/69 - 4/30/69	30	10.8390	0.4810
5/ 1/69 - 5/31/69	31	10.1565	0.6112
6/ 1/69 - 6/30/69	30	9.9767	0.7278
7/ 1/69 - 7/31/69	31	10.2965	0.7100
8/ 1/69 - 8/31/69	31	10.4761	0.6406
9/ 1/69 - 9/30/69	30	9.7290	0.5017
10/ 1/69 - 10/31/69	31	10.0545	0.4867
11/ 1/69 - 11/30/69	30	10.1233	0.4409
12/ 1/69 - 12/31/69	31	10.3842	0.5963
1/ 1/70 - 1/31/70	31	10.3281	0.6198
2/ 1/70 - 2/28/70	28	10.1696	0.5316
3/ 1/70 - 4/ 2/70	31	10.1761	0.6594

N = 24

$\bar{x}$ = 9.70

S.D. = 1.10

Table 2 - Monthly means and the grand mean for the analytical concentrations of lead chlorobromide in Group III.

<u>Date</u>	<u>n</u>	<u>$\bar{x}$</u> <u>mg/m³</u>	<u>S.D.</u>
5/11/68 - 5/31/68	20	0.8570	1.0552
6/ 1/68 - 6/30/68	30	0.4743	0.6379
7/ 1/68 - 7/31/68	31	0.4565	0.3048
8/ 1/68 - 8/31/68	31	0.6022	0.1088
9/ 1/68 - 9/30/68	30	0.5773	0.1526
10/ 1/68 - 10/31/68	31	0.5074	0.1497
11/ 1/68 - 11/30/68	30	0.4286	0.1944
12/ 1/68 - 12/31/68	31	0.4638	0.1819
1/ 1/69 - 1/31/69	31	0.4752	0.1339
2/ 1/69 - 2/28/69	28	0.6154	0.7173
3/ 1/69 - 3/31/69	31	0.5677	0.1515
4/ 1/69 - 4/30/69	30	0.5147	0.2131
5/ 1/69 - 5/31/69	31	0.7770	0.1710
6/ 1/69 - 6/30/69	30	0.5503	0.1740
7/ 1/69 - 7/31/69	31	0.5597	0.2216
8/ 1/69 - 8/31/69	31	0.5010	0.1545
9/ 1/69 - 9/30/69	30	0.4737	0.2049
10/ 1/69 - 10/31/69	31	0.5352	0.2722
11/ 1/69 - 11/30/69	30	0.4930	0.0363
12/ 1/69 - 12/31/69	31	0.3871	0.1065
1/ 1/70 - 1/31/70	31	0.4052	0.2503
2/ 1/70 - 2/28/70	28	0.5100	0.3669
3/ 1/70 - 3/31/70	31	0.5561	0.2526
4/ 1/70 - 4/30/70	30	0.3070	0.5232
5/ 1/70 - 5/ 5/70	5	0.1080	0.0295

N = 25

$\bar{x}$ = 0.51

S.D. = 0.27

Table 3 - Monthly means and the grand mean for the analytical concentrations of sulfur dioxide and lead chlorobromide for Group IV.

Date	n	SO ₂		PbClBr	
		$\bar{x}$ ppm	S.D.	$\bar{x}$ mg/m ³	S.D.
6/ 1/68 - 6/30/68	30	9.0860	1.2098	0.7460	0.6084
7/ 1/68 - 7/31/68	31	9.4800	1.5272	0.6381	0.3021
8/ 1/68 - 8/31/68	31	8.1126	2.3330	0.5897	0.1578
9/ 1/68 - 9/30/68	30	8.1710	1.8994	0.4690	0.3260
10/ 1/68 - 10.31/68	31	9.8820	9.2737	0.4271	0.1582
11/ 1/68 - 11/30/68	30	9.8613	0.9160	0.3920	0.1834
12/ 1/68 - 12/31/68	31	10.1381	1.2822	0.4500	0.1752
1/ 1/69 - 1/31/69	31	8.1694	2.2516	0.4755	0.1776
2/ 1/69 - 2/28/69	28	9.9996	0.9223	0.5825	0.3086
3/ 1/69 - 3/31/69	31	9.8535	1.4923	0.6377	0.2419
4/ 1/69 - 4/30/69	30	10.6361	2.0651	0.5557	0.2620
5/ 1/69 - 5/31/69	31	10.2061	0.6014	0.6194	0.1859
6/ 1/69 - 6/30/69	30	10.0123	0.7646	0.6340	0.2501
7/ 1/69 - 7/31/69	31	10.2297	0.7385	0.4252	0.1405
8/ 1/69 - 8/31/69	31	10.5742	0.6935	0.4516	0.2649
9/ 1/69 - 9/30/69	30	9.9700	0.5091	0.4090	0.1720
10/ 1/69 - 10/31/69	31	10.1168	9.4745	0.3925	0.2516
11/ 1/69 - 11/30/69	30	10.2610	0.3675	0.4333	0.1563
12/ 1/69 - 12/31/69	31	10.4919	0.3204	0.5413	0.2833
1/ 1/70 - 1/31/70	31	10.5181	0.4787	0.5906	0.3867
2/ 1/70 - 2/28/70	28	10.4392	0.3408	0.5257	0.9777
3/ 1/70 - 3/31/70	31	10.4284	0.4740	0.5903	0.2595
4/ 1/70 - 4/30/70	30	10.8520	0.2919	0.2017	0.0730
5/ 1/70 - 5/12/70	12	10.8500	0.4373	0.2417	0.1083

N = 24

$\bar{x}$ = 9.93

S.D. = 1.03

N = 24

$\bar{x}$ = 0.50

S.D. = 0.27

Table 4 - Summary of statistical analyses of body weight data for Statistical Grouping C, comprised of the following: Group I - Control, Group II - 9.70 ppm SO₂, Group III - 0.51 mg/m³ pbcIb_r, and Group IV - 9.93 ppm SO₂ + 0.50 mg/m³ pbcIb_r.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	2.908	9.693 × 10 ⁻¹	0.96	-
Error Deviation	886	8.892 × 10 ²	1.004	-	-

FIRST DEGREE POLYNOMIAL REGRESSION COEFFICIENTS					
GROUPS	REGRESSION COEFFICIENTS		S.E.	Sy.x	r
	A	B			
I	2.63 ± 0.052	1.64 × 10 ⁻² ± 8.93 × 10 ⁻⁴	0.14	33	0.96
II	2.95 ± 0.053	1.13 × 10 ⁻² ± 8.91 × 10 ⁻⁴	0.14	30	0.94
III	2.61 ± 0.046	1.53 × 10 ⁻² ± 8.02 × 10 ⁻⁴	0.13	27	0.97
IV	2.62 ± 0.055	1.45 × 10 ⁻² ± 9.23 × 10 ⁻⁴	0.14	31	0.96

Table 5 - Summary of statistical analyses of total respiratory system flow resistance during inspiration data for Statistical Grouping C, comprised of the following: Group I - Control, Group II - 9.70 ppm SO₂, Group III - 0.51 mg/m³ PbClBr, and Group IV - 9.93 ppm SO₂ + 0.50 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	1.045 x 10 ⁻³	3.482 x 10 ⁻⁴	2.69	Yes
Error Deviation	1119	1.446 x 10 ⁻¹	1.292 x 10 ⁻⁴	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.					Sy.x	n	r
	A	B	C	D				
I	0.014 ± 0.0033	2.12 x 10 ⁻⁴ ± 3.81 x 10 ⁻⁴	-9.72 x 10 ⁻⁶ ± 9.30 x 10 ⁻⁶	8.10 x 10 ⁻⁸ ± 6.10 x 10 ⁻⁸		0.008	39	0.37
II	0.043 ± 0.0029	-7.21 x 10 ⁻⁵ ± 3.34 x 10 ⁻⁴	1.50 x 10 ⁻⁶ ± 8.10 x 10 ⁻⁶	-7.00 x 10 ⁻⁹ ± 5.30 x 10 ⁻⁸		0.007	38	0.08
III	0.053 ± 0.0026	-5.51 x 10 ⁻⁴ ± 3.01 x 10 ⁻⁴	5.41 x 10 ⁻⁶ ± 7.35 x 10 ⁻⁶	-2.00 x 10 ⁻⁹ ± 4.80 x 10 ⁻⁸		0.006	39	0.65
IV	0.046 ± 0.002	-2.45 x 10 ⁻⁴ ± 3.36 x 10 ⁻⁴	4.49 x 10 ⁻⁶ ± 8.56 x 10 ⁻⁶	-1.90 x 10 ⁻⁸ ± 5.80 x 10 ⁻⁸		0.006	36	0.25

Table 6 - Summary of statistical analyses of total respiratory system flow resistance during expiration data for Statistical Grouping C, comprised of the following: Group I - Control, Group II - 9.70 ppm SO₂, Group III - 0.51 mg/m³ PbClBr, and Group IV - 9.93 ppm SO₂ + 0.50 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	1.157 x 10 ⁻³	3.857 x 10 ⁻⁴	3.84	Yes
Error Deviation	1119	1.124 x 10 ⁻¹	1.005 x 10 ⁻⁴	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.					Sy.x	n	r
	A	B	C	D				
I	0.042 ± 0.0028	-2.07 x 10 ⁻⁴ ± 3.26 x 10 ⁻⁴	-1.34 x 10 ⁻⁶ ± 7.97 x 10 ⁻⁶	2.90 x 10 ⁻⁸ ± 5.20 x 10 ⁻⁸		0.007	39	0.55
II	0.040 ± 0.0025	-3.48 x 10 ⁻⁴ ± 2.90 x 10 ⁻⁴	5.82 x 10 ⁻⁶ ± 7.02 x 10 ⁻⁶	-2.90 x 10 ⁻⁸ ± 4.60 x 10 ⁻⁸		0.006	38	0.36
III	0.046 ± 0.0023	-5.02 x 10 ⁻⁴ ± 2.70 x 10 ⁻⁴	7.29 x 10 ⁻⁶ ± 6.61 x 10 ⁻⁶	1.90 x 10 ⁻⁸ ± 4.30 x 10 ⁻⁸		0.005	39	0.67
IV	0.040 ± 0.0024	-3.82 x 10 ⁻⁴ ± 2.86 x 10 ⁻⁴	7.76 x 10 ⁻⁶ ± 7.29 x 10 ⁻⁶	-4.20 x 10 ⁻⁸ ± 4.93 x 10 ⁻⁸		0.005	35	0.30

Table 7 - Summary of statistical analyses of tidal volume data for Statistical Grouping C, comprised of the following: Group I - Control, Group II - 9.70 ppm SO₂, Group III - 0.51 mg/m³ PbClBr, and Group IV - 9.93 ppm SO₂ + 0.50 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	9.489 x 10 ⁺¹	3.163 x 10 ⁺¹	0.26	-
Error Deviation	879	1.047 x 10 ⁺⁵	1.191 x 10 ⁺²	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.					n	r
	A	B	C	D	Sy.x		
I	28.72 ± 1.92	2.52 x 10 ⁻¹ ± 1.88 x 10 ⁻¹	-2.46 x 10 ⁻³ ± 4.42 x 10 ⁻³	1.16 x 10 ⁻⁵ ± 2.84 x 10 ⁻⁵	3.48	32	0.77
II	32.29 ± 2.02	3.08 x 10 ⁻¹ ± 1.94 x 10 ⁻¹	-4.07 x 10 ⁻³ ± 4.54 x 10 ⁻³	2.04 x 10 ⁻⁵ ± 2.90 x 10 ⁻⁵	3.67	32	0.68
III	31.10 ± 1.75	1.64 x 10 ⁻² ± 1.72 x 10 ⁻¹	5.87 x 10 ⁻⁴ ± 4.10 x 10 ⁻³	3.80 x 10 ⁻⁶ ± 2.64 x 10 ⁻⁵	3.20	31	0.79
IV	27.50 ± 1.70	3.50 x 10 ⁻¹ ± 1.64 x 10 ⁻¹	-3.23 x 10 ⁻³ ± 3.91 x 10 ⁻³	8.10 x 10 ⁻⁶ ± 2.57 x 10 ⁻⁵	2.81	28	0.82

Table 8 - Summary of statistical analyses of respiratory rate data for Statistical Grouping C, comprised of the following: Group I - Control, Group II - 9.70 ppm SO₂, Group III - 0.51 mg/m³ PbClBr, and Group IV - 9.93 ppm SO₂ + 0.50 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	7.452 x 10 ⁺²	2.484 x 10 ⁺²	3.93	Yes
Lack of Deviation	879	5.551 x 10 ⁺⁴	6.315 x 10 ⁺¹	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.					Sy.X	n	r
	A	B	C	D				
I	40.74 ± 1.26	3.16 x 10 ⁻¹ ± 1.23 x 10 ⁻¹	-9.30 x 10 ⁻³ ± 2.90 x 10 ⁻³	5.63 x 10 ⁻⁵ ± 1.86 x 10 ⁻⁵		2.29	32	0.84
II	38.90 ± 1.38	2.08 x 10 ⁻¹ ± 1.32 x 10 ⁻¹	-5.91 x 10 ⁻³ ± 3.09 x 10 ⁻³	3.58 x 10 ⁻⁵ ± 1.98 x 10 ⁻⁵		2.50	32	0.63
III	37.85 ± 1.83	2.67 x 10 ⁻¹ ± 1.80 x 10 ⁻¹	-4.08 x 10 ⁻³ ± 4.28 x 10 ⁻³	1.39 x 10 ⁻⁵ ± 2.76 x 10 ⁻⁵		3.34	31	0.51
IV	42.94 ± 1.18	1.40 x 10 ⁻¹ ± 1.13 x 10 ⁻¹	-4.12 x 10 ⁻³ ± 2.70 x 10 ⁻³	2.38 x 10 ⁻⁵ ± 1.78 x 10 ⁻⁵		1.94	28	0.71

Table 9 - Summary of statistical analysis of dynamic compliance of the lung data for Statistical Grouping C, comprised of the following: Group I - Control, Group II - 9.70 ppm SO₂, Group III - 0.51 mg/m³ PbClBr, and Group IV - 9.93 ppm SO₂ + 0.50 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	5.902 x 10 ⁺¹	1.967 x 10 ⁺¹	3.54	Yes
Error Deviation	879	4.889 x 10 ⁺³	5.563	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.				Sv.x	n	r
	A	B	C	D			
I	6.11 ± 0.46	1.83 x 10 ⁻² ± 4.55 x 10 ⁻²	-1.88 x 10 ⁻⁴ ± 1.07 x 10 ⁻³	1.30 x 10 ⁻⁶ ± 6.90 x 10 ⁻⁶	0.84	32	0.43
II	8.07 ± 0.87	-6.98 x 10 ⁻³ ± 8.37 x 10 ⁻²	4.10 x 10 ⁻⁴ ± 1.96 x 10 ⁻³	-3.30 x 10 ⁻⁶ ± 1.25 x 10 ⁻⁵	1.58	32	0.11
III	6.09 ± 0.57	6.22 x 10 ⁻² ± 5.65 x 10 ⁻²	-1.12 x 10 ⁻³ ± 1.34 x 10 ⁻³	6.80 x 10 ⁻⁶ ± 8.70 x 10 ⁻⁶	1.05	31	0.45
IV	5.49 ± 0.43	-1.64 x 10 ⁻² ± 4.13 x 10 ⁻²	1.35 x 10 ⁻³ ± 9.87 x 10 ⁻⁴	-1.01 x 10 ⁻⁵ ± 6.50 x 10 ⁻⁶	0.71	28	0.80

Table 10 - Summary of statistical analyses of pulmonary flow resistance data for Statistical Grouping C, comprised of the following: Group I - Control, Group II - 9.70 ppm SO₂, Group III - 0.51 mg/m³ PbClBr, and Group IV - 9.93 ppm SO₂ + 0.50 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	1.755 × 10 ⁻³	5.850 × 10 ⁻⁴	4.05	Yes
Error Deviation	879	1.269 × 10 ⁻¹	1.443 × 10 ⁻⁴	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.					Sy.x	n	r
	A	B	C	D				
I	0.024 ± 0.0036	7.84 × 10 ⁻⁵ ± 3.53 × 10 ⁻⁴	8.71 × 10 ⁻⁷ ± 8.32 × 10 ⁻⁶	-1.80 × 10 ⁻⁸ ± 5.30 × 10 ⁻⁸		0.006	32	0.28
II	0.019 ± 0.0032	3.54 × 10 ⁻⁴ ± 3.13 × 10 ⁻⁴	-9.10 × 10 ⁻⁶ ± 7.32 × 10 ⁻⁶	5.29 × 10 ⁻⁸ ± 4.70 × 10 ⁻⁸		0.006	32	0.48
III	0.025 ± 0.0039	8.94 × 10 ⁻⁶ ± 3.82 × 10 ⁻⁴	-7.73 × 10 ⁻⁷ ± 9.10 × 10 ⁻⁶	-3.00 × 10 ⁻⁹ ± 5.90 × 10 ⁻⁸		0.007	31	0.45
IV	0.026 ± 0.0031	2.72 × 10 ⁻⁴ ± 2.97 × 10 ⁻⁴	-9.95 × 10 ⁻⁶ ± 7.09 × 10 ⁻⁶	6.60 × 10 ⁻⁸ ± 4.70 × 10 ⁻⁸		0.005	28	0.65

Table 11 - Summary of statistical analyses of work of breathing during inspiration per ml tidal volume data for Statistical Grouping C, comprised of the following: Group I - Control, Group II - 9.70 ppm SO₂, Group III - 0.51 mg/m³ PbClBr, and Group IV - 9.93 ppm SO₂ + 0.50 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	1.701 x 10 ⁺¹	5.670	3.39	Yes
Error Deviation	878	1.467 x 10 ⁺³	1.671	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.						n	r
	A	B	C	D	Sy.x			
I	3.94 ± 0.30	-2.00 x 10 ⁻² ± 2.97 x 10 ⁻²	5.07 x 10 ⁻⁴ ± 7.00 x 10 ⁻⁴	-2.90 x 10 ⁻⁶ ± 4.50 x 10 ⁻⁶	0.55		32	0.25
II	3.36 ± 0.42	1.74 x 10 ⁻² ± 4.05 x 10 ⁻²	-6.45 x 10 ⁻⁴ ± 9.48 x 10 ⁻⁴	5.20 x 10 ⁻⁶ ± 6.10 x 10 ⁻⁶	0.77		32	0.27
III	4.13 ± 0.36	-7.57 x 10 ⁻² ± 3.54 x 10 ⁻²	1.49 x 10 ⁻³ ± 8.43 x 10 ⁻³	-7.90 x 10 ⁻⁶ ± 5.40 x 10 ⁻⁶	0.66		31	0.46
IV	4.23 ± 0.40	-1.94 x 10 ⁻⁴ ± 3.86 x 10 ⁻²	-3.73 x 10 ⁻⁴ ± 9.23 x 10 ⁻⁴	3.30 x 10 ⁻⁶ ± 6.10 x 10 ⁻⁶	0.66		28	0.41

Table 12 - Summary of statistical analyses of work of breathing during expiration per ml tidal volume data for Statistical Grouping C, comprised of the following: Group I - Control; Group II - 9.70 ppm SO₂, Group III - 0.51 mg/m³ PbClBr, and Group IV - 9.93 ppm SO₂ + 0.50 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	9.244 × 10 ⁻¹	3.081 × 10 ⁻¹	0.99	-
Error Deviation	878	2.723 × 10 ⁺²	3.101 × 10 ⁻¹	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.					n	r
	A	B	C	D	Sy.x		
I	1.85 ± 0.16	-2.66 × 10 ⁻² ± 1.60 × 10 ⁻²	5.49 × 10 ⁻⁴ ± 3.76 × 10 ⁻⁴	-3.00 × 10 ⁻⁶ ± 2.40 × 10 ⁻⁶	0.30	32	0.36
II	1.60 ± 0.15	-1.55 × 10 ⁻² ± 1.50 × 10 ⁻²	2.82 × 10 ⁻⁴ ± 3.50 × 10 ⁻⁴	-1.20 × 10 ⁻⁶ ± 2.20 × 10 ⁻⁶	0.28	32	0.34
III	1.73 ± 0.16	-2.15 × 10 ⁻² ± 1.57 × 10 ⁻²	3.97 × 10 ⁻⁴ ± 3.74 × 10 ⁻⁴	-1.80 × 10 ⁻⁶ ± 2.40 × 10 ⁻⁶	0.29	31	0.39
IV	1.78 ± 0.16	-3.43 × 10 ⁻³ ± 1.54 × 10 ⁻²	-3.64 × 10 ⁻⁵ ± 3.69 × 10 ⁻⁴	6.00 × 10 ⁻⁷ ± 2.40 × 10 ⁻⁶	0.26	28	0.27

Table 13 - Summary of statistical analyses of diffusing capacity of the lung for carbon monoxide data for Statistical Grouping C, comprised of the following: Group I - Control, Group II - 9.70 ppm SO₂, Group III - 0.51 mg/m³ PbClBr, and Group IV - 9.93 ppm SO₂ + 0.50 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	9.553 x 10 ⁻²	3.184 x 10 ⁻²	1.29	-
Error Deviation	886	2.185 x 10 ⁻¹	2.466 x 10 ⁻²	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.					Sv.x	n	r
	A	B	C	D	U			
I	0.62 ± 0.031	3.04 x 10 ⁻³ ± 2.91 x 10 ⁻³	-2.49 x 10 ⁻⁵ ± 7.00 x 10 ⁻⁵	1.50 x 10 ⁻⁷ ± 4.60 x 10 ⁻⁷		0.052	33	0.78
II	0.72 ± 0.042	-1.08 x 10 ⁻³ ± 4.10 x 10 ⁻³	4.16 x 10 ⁻⁵ ± 9.69 x 10 ⁻⁵	-1.90 x 10 ⁻⁷ ± 6.30 x 10 ⁻⁷		0.069	30	0.58
III	0.67 ± 0.052	-3.33 x 10 ⁻³ ± 4.83 x 10 ⁻³	1.26 x 10 ⁻⁴ ± 1.16 x 10 ⁻⁴	-7.50 x 10 ⁻⁷ ± 7.70 x 10 ⁻⁷		0.087	33	0.68
IV	0.70 ± 0.034	-1.90 x 10 ⁻³ ± 3.29 x 10 ⁻³	7.41 x 10 ⁻⁵ ± 7.87 x 10 ⁻⁵	-3.70 x 10 ⁻⁷ ± 5.20 x 10 ⁻⁷		0.057	31	0.78

Table 14 - Summary of statistical analyses of number of breaths to 1% nitrogen data for Statistical Grouping C, comprised of the following: Group I - Control, Group II - 9.70 ppm SO₂, Group III - 0.51 mg/m³ PbClBr, and Group IV - 9.93 ppm SO₂ + 0.50 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	5.188 x 10 ⁺²	1.729 x 10 ⁺²	1.08	-
Error Deviation	884	1.413 x 10 ⁺⁵	1.598 x 10 ⁺²	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.					Sy.x	n	r
	A	B	C	D				
I	42.85 ± 3.42	8.85 x 10 ⁻² ± 3.26 x 10 ⁻¹	1.08 x 10 ⁻³ ± 7.83 x 10 ⁻³	-2.10 x 10 ⁻⁵ ± 5.20 x 10 ⁻⁵		5.69	32	0.33
II	41.79 ± 3.01	2.96 x 10 ⁻¹ ± 2.95 x 10 ⁻¹	-6.92 x 10 ⁻³ ± 6.99 x 10 ⁻³	4.90 x 10 ⁻⁵ ± 4.50 x 10 ⁻⁵		4.96	30	0.44
III	44.77 ± 3.08	2.51 x 10 ⁻¹ ± 2.93 x 10 ⁻¹	1.16 x 10 ⁻³ ± 7.06 x 10 ⁻³	-3.40 x 10 ⁻⁵ ± 4.70 x 10 ⁻⁵		5.16	32	0.64
IV	37.88 ± 2.36	1.85 x 10 ⁻¹ ± 2.22 x 10 ⁻¹	2.59 x 10 ⁻³ ± 5.39 x 10 ⁻³	-4.70 x 10 ⁻⁵ ± 3.60 x 10 ⁻⁵		3.96	31	0.73

Table 15 - Summary of statistical analyses of respiratory rate (during oxygen breathing) data for Statistical Grouping C, comprised of the following: Group I - Control, Group II - 9.70 ppm SO₂, Group III - 0.51 mg/m³ PbClBr, and Group IV - 9.93 ppm SO₂ + 0.50 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	5.070 x 10 ⁺²	1.690 x 10 ⁺²	2.45	-
Error Deviation	884	6.087 x 10 ⁺⁴	6.886 x 10 ⁺¹	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.					Sv. x	h	r
	A	B	C	D				
I	34.46 ± 1.11	2.49 x 10 ⁻¹ ± 1.06 x 10 ⁻¹	-9.27 x 10 ⁻³ ± 2.54 x 10 ⁻³	6.52 x 10 ⁻⁵ ± 1.68 x 10 ⁻⁵		1.84	32	0.86
II	34.42 ± 1.51	2.48 x 10 ⁻¹ ± 1.48 x 10 ⁻¹	-7.12 x 10 ⁻³ ± 3.51 x 10 ⁻³	4.36 x 10 ⁻⁵ ± 2.28 x 10 ⁻⁵		2.50	30	0.70
III	33.38 ± 1.80	1.91 x 10 ⁻¹ ± 1.71 x 10 ⁻¹	-2.86 x 10 ⁻³ ± 4.13 x 10 ⁻³	7.40 x 10 ⁻⁶ ± 2.72 x 10 ⁻⁶		3.02	32	0.52
IV	38.94 ± 1.77	-6.47 x 10 ⁻² ± 1.67 x 10 ⁻¹	8.83 x 10 ⁻⁴ ± 4.05 x 10 ⁻³	-5.40 x 10 ⁻⁶ ± 2.53 x 10 ⁻⁵		2.97	31	0.30

Table 16 - Summary of statistical analyses of cumulative tidal volume to 1% nitrogen data for Statistical Grouping C, comprised of the following: Group I - Control, Group II - 9.70 ppm SO₂, Group III - 0.51 mg/m³ PbClBr, and Group IV - 9.93 ppm SO₂ + 0.50 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	3.947 × 10 ⁻¹	1.316 × 10 ⁻¹	0.81	-
Error Deviation	884	1.426 × 10 ⁺²	1.613 × 10 ⁻¹	-	-

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THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.					Sy.x	n	r
	A	B	C	D				
I	1.35 ± 0.094	5.79 × 10 ⁻³ ± 8.95 × 10 ⁻³	-1.38 × 10 ⁻⁵ ± 2.15 × 10 ⁻⁴	0.00 ± 1.40 × 10 ⁻⁶		0.16	32	0.70
II	1.53 ± 0.108	1.50 × 10 ⁻³ ± 1.06 × 10 ⁻²	5.12 × 10 ⁻⁵ ± 2.52 × 10 ⁻⁴	-4.00 × 10 ⁻⁷ ± 1.60 × 10 ⁻⁶		0.18	30	0.52
III	1.52 ± 0.074	4.55 × 10 ⁻⁴ ± 7.04 × 10 ⁻³	2.09 × 10 ⁻⁴ ± 1.70 × 10 ⁻⁴	-1.80 × 10 ⁻⁶ ± 1.10 × 10 ⁻⁶		0.12	32	0.82
IV	1.25 ± 0.081	-2.85 × 10 ⁻³ ± 7.65 × 10 ⁻³	3.42 × 10 ⁻⁴ ± 1.85 × 10 ⁻⁴	-2.90 × 10 ⁻⁶ ± 1.20 × 10 ⁻⁶		0.14	31	0.81

Table 17 - Summary of statistical analyses of tidal volume (during oxygen breathing) data for Statistical Grouping C, comprised of the following: Group I - Control, Group II - 9.70 ppm SO₂, Group III - 0.51 mg/m³ PbClBr, and Group IV - 9.93 ppm SO₂ + 0.50 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	1.125 x 10 ⁺³	3.751 x 10 ⁺²	4.00	Yes
Error Deviation	884	8.284 x 10 ⁺⁴	9.371 x 10 ⁺¹	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.				Sv. x	n	r
	A	B	C	D			
I	39.08 ± 2.58	2.20 x 10 ⁻¹ ± 2.47 x 10 ⁻¹	-5.34 x 10 ⁻³ ± 5.92 x 10 ⁻³	4.68 x 10 ⁻⁵ ± 3.91 x 10 ⁻⁵	4.30	32	0.70
II	45.45 ± 2.10	-1.52 x 10 ⁻¹ ± 2.07 x 10 ⁻¹	5.46 x 10 ⁻³ ± 4.89 x 10 ⁻³	-4.01 x 10 ⁻⁵ ± 3.13 x 10 ⁻⁵	3.47	30	0.38
III	43.09 ± 2.17	-1.77 x 10 ⁻¹ ± 2.07 x 10 ⁻¹	3.84 x 10 ⁻³ ± 4.97 x 10 ⁻³	-1.63 x 10 ⁻⁵ ± 3.28 x 10 ⁻⁵	3.64	32	0.53
IV	41.72 ± 1.93	-2.38 x 10 ⁻¹ ± 1.82 x 10 ⁻¹	6.50 x 10 ⁻³ ± 4.40 x 10 ⁻³	-3.35 x 10 ⁻⁵ ± 2.92 x 10 ⁻⁵	3.24	31	0.76

Table 18 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for hematotcrit (Hct. - percent) for male and female monkeys in Statistical Grouping C.

Groups	Time-Weeks			
	Pre-exposure -8	4	16	68
I - Control	36.4 (0.8)	36.0 (1.0)	33.1 (1.0)	37.3 (1.0)
II - 9.70 ppm SO ₂	35.0 (0.7)	35.0 (0.6)	34.0 (0.6)	36.4 (0.6)
III - 0.51 mg/m ³ PbCl ₂	32.3 (0.8)	35.8 (0.8)	34.3 (0.9)	35.4 (1.1)
IV - 9.93 ppm SO ₂ + 0.50 mg m ³ PbCl ₂	34.2 (1.2)	33.8 (1.4)	34.1 (1.1)	37.8 (1.2)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks			
	Pre-exposure -8	4	16	68
Pb	SIG	N.S.	N.S.	N.S.
SO ₂	N.S.	N.S.	N.S.	N.S.
Interaction	N.S.	N.S.	N.S.	N.S.

Table 19 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for hemoglobin (Hgb. - grams percent) for male and female monkeys in Statistical Grouping C.

Groups	Pre-exposure -8	Time-Weeks			
		4	16	68	104
I - Control	10.5 (0.3)	11.0 (0.3)	11.2 (0.2)	10.7 (0.3)	11.7 (0.3)
II - 9.70 ppm SO ₂	10.5 (0.2)	10.6 (0.2)	10.1 (0.2)	11.0 (0.2)	10.9 (0.2)
III - 0.51 mg/m ³ PbClBr	10.2 (0.2)	9.8 (0.2)	10.4 (0.2)	10.4 (0.3)	10.6 (0.3)
IV - 9.93 ppm SO ₂ + 0.50 mg/m ³ PbClBr	9.8 (0.3)	11.1 (0.5)	11.1 (0.3)	11.2 (0.4)	11.2 (0.4)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Pre-exposure -8	Time-Weeks			
		4	16	68	104
Pb	SIG	N.S.	N.S.	N.S.	N.S.
SO ₂	N.S.	N.S.	N.S.	N.S.	N.S.
Interaction	N.S.	SIG	SIG	N.S.	SIG

Table 20 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for total erythrocyte count (RBC - $10^6/\text{cmm}$) for male and female monkeys in Statistical Grouping C.

Groups	Time-Weeks			
	Pre-exposure -8	4	16	68
I - Control	5.44 (0.09)	5.44 (0.18)	5.70 (0.22)	5.10 (0.13)
II - 9.70 ppm SO ₂	5.08 (0.08)	5.20 (0.14)	4.98 (0.12)	5.39 (0.11)
III - 0.51 mg/m ³ PbClBr	5.13 (0.18)	4.89 (0.20)	5.39 (0.30)	5.64 (0.23)
IV - 9.93 ppm SO ₂ + 0.50 mg/m ³ PbClBr	5.00 (0.21)	5.20 (0.17)	5.06 (0.23)	5.52 (0.25)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks			
	Pre-exposure -8	4	16	68
Pb	SIG	N.S.	N.S.	N.S.
SO ₂	SIG	N.S.	SIG	SIG
Interaction	N.S.	N.S.	N.S.	N.S.

Table 21 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for total leukocyte count (WBC - per cmm) for male and female monkeys in Statistical Grouping C.

Groups	Time-Weeks					
	Pre-exposure	-8	4	16	68	104
I - Control		7240 (840)	7170 (290)	8670 (710)	8220 (680)	11940 (1110)
II - 9.70 ppm SO ₂		9140 (720)	10110 (1160)	14260 (1210)	11680 (680)	9410 (740)
III - 0.51 mg/m ³ PbClBr		8430 (860)	11040 (3060)	9700 (930)	9110 (850)	8420 (870)
IV - 9.93 ppm SO ₂ + 0.50 mg/m ³ PbClBr		6430 (940)	8510 (700)	10530 (940)	9060 (730)	8510 (1400)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks					
	Pre-exposure	-8	4	16	68	104
Pb	N.S.		N.S.	N.S.	N.S.	SIG
SO ₂	N.S.		N.S.	SIG	SIG	N.S.
Interaction	SIG		N.S.	SIG	SIG	N.S.

Table 22 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for blood glucose (Glu. - mg percent) for male and female monkeys in Statistical Grouping C.

Groups	Time-Weeks				
	Pre-exposure -8	4	16	68	104
I - Control	59.3 (3.3)	59.5 (3.3)	69.0 (4.4)	97.3 (5.3)	82.4 (7.5)
II - 9.70 ppm SO ₂	61.3 (1.6)	75.3 (3.6)	76.8 (5.7)	86.6 (6.0)	71.6 (5.3)
III - 0.51 mg/m ³ PbClBr	68.3 (2.9)	52.0 (3.0)	80.0 (2.2)	93.4 (3.5)	87.3 (5.2)
IV - 9.93 ppm SO ₂ + 0.50 mg/m ³ PbClBr	72.8 (2.1)	104.7 (9.0)	75.2 (6.9)	63.4 (2.7)	80.5 (7.6)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks				
	Pre-exposure -8	4	16	68	104
Pb	SIG	N.S.	N.S.	SIG	N.S.
SO ₂	N.S.	SIG	N.S.	SIG	N.S.
Interaction	N.S.	SIG	N.S.	SIG	N.S.

Table 23 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for blood urea nitrogen (BUN - mg percent) for male and female monkeys in Statistical Grouping C.

Groups	Time-Weeks			
	Pre-exposure -8	4	16	68
I - Control	16.3 (1.0)	19.2 (1.4)	17.0 (0.6)	22.6 (0.7)
II - 9.70 ppm SO ₂	18.7 (1.5)	14.1 (1.0)	15.4 (0.7)	19.1 (1.8)
III - 0.51 mg/m ³ PbClBr	14.4 (0.6)	15.8 (0.5)	8.8 (0.9)	22.6 (1.6)
IV - 9.93 ppm SO ₂ + 0.50 mg/m ³ PbClBr	17.4 (1.0)	25.5 (3.5)	28.8 (1.6)	25.9 (1.8)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks			
	Pre-exposure -8	4	16	68
Pb	N.S.	SIG	SIG	SIG
SO ₂	SIG	N.S.	SIG	N.S.
Interaction	N.S.	SIG	SIG	SIG

Table 24 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for total serum bilirubin (mg percent) for male and female monkeys in Statistical Grouping C.

Groups	Time-Weeks				
	Pre-exposure -8	4	16	68	104
I - Control	0.27 (0.03)	0.26 (0.02)	0.26 (0.02)	0.29 (0.03)	0.50 (0.06)
II - 9.70 ppm SO ₂	0.27 (0.02)	0.21 (0.02)	0.41 (0.04)	0.24 (0.02)	0.30 (0.01)
III - 0.51 mg/m ³ PbClBr	0.18 (0.01)	0.28 (0.02)	0.28 (0.02)	0.27 (0.01)	0.33 (0.01)
IV - 9.93 ppm SO ₂ + 0.50 mg/m ³ PbClBr	0.60 (0.08)	0.70 (0.12)	0.40 (0.06)	0.54 (0.05)	0.37 (0.03)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks				
	Pre-exposure -8	4	16	68	104
Pb	SIG	SIG	N.S.	SIG	N.S.
SO ₂	SIG	SIG	SIG	SIG	N.S.
Interaction	SIG	SIG	N.S.	SIG	SIG

Table 25 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for total serum protein (grams percent) for male and female monkeys in Statistical Grouping C.

Groups	Time-Weeks				
	Pre-exposure -8	4	16	68	104
I - Control	7.30 (0.13)	7.76 (0.13)	8.24 (0.10)	7.44 (0.13)	7.56 (0.09)
II - 9.70 ppm SO ₂	7.57 (0.12)	7.30 (0.12)	7.61 (0.06)	7.61 (0.06)	7.47 (0.11)
III - 0.51 mg/m ³ PbClBr	7.53 (0.17)	7.74 (0.19)	7.75 (0.22)	7.00 (0.13)	7.29 (0.16)
IV - 9.93 ppm SO ₂ + 0.50 mg/m ³ PbClBr	7.62 (0.08)	8.02 (0.14)	8.00 (0.20)	7.56 (0.19)	6.90 (0.11)

Comparison of Experimental Treatment Effects ($p < .05$)

Source of Variation	Time-Weeks				
	Pre-exposure -8	4	16	68	104
Pb	N.S.	SIG	N.S.	N.S.	SIG
SO ₂	N.S.	N.S.	N.S.	SIG	N.S.
Interaction	N.S.	SIG	SIG	N.S.	N.S.

Table 26 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for serum albumin (grams percent) for male and female monkeys in Statistical Grouping C.

Groups	Time-Weeks			
	Pre-exposure -8	4	16	68
I - Control	2.56 (0.14)	2.58 (0.05)	3.11 (0.06)	2.45 (0.11)
II - 9.70 ppm SO ₂	2.24 (0.15)	2.57 (0.11)	2.53 (0.05)	2.88 (0.05)
III - 0.51 mg/m ³ PbClBr	2.41 (0.05)	2.30 (0.05)	2.49 (0.04)	2.56 (0.05)
IV - 9.93 ppm SO ₂ + 0.50 mg/m ³ PbClBr	2.51 (0.08)	3.32 (0.08)	2.56 (0.08)	2.76 (0.06)

Comparison of Experimental Treatment Effects ($p < .05$)

Source of Variation	Time-Weeks			
	Pre-exposure -8	4	16	68
Pb	N.S.	SIG	SIG	N.S.
SO ₂	N.S.	N.S.	SIG	N.S.
Interaction	N.S.	SIG	SIG	N.S.

Table 27 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for total sodium (Na - mEq/liter) for male and female monkeys in Statistical Grouping C.

Groups	Time-Weeks				
	Pre-exposure -8	4	16	68	104
I - Control	148.0 (0.5)	143.7 (0.3)	139.2 (0.6)	145.8 (0.8)	148.7 (0.6)
II - 9.70 ppm SO ₂	150.4 (0.8)	141.0 (0.7)	140.9 (0.4)	145.0 (0.4)	146.9 (0.3)
III - 0.51 mg/m ³ PbClBr	147.1 (0.4)	145.0 (0.6)	141.8 (0.5)	148.0 (0.8)	148.5 (0.5)
IV - 9.93 ppm SO ₂ + 0.50 mg/m ³ PbClBr	140.5 (0.6)	145.2 (0.9)	141.8 (0.5)	148.0 (0.7)	147.9 (0.4)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks				
	Pre-exposure -8	4	16	68	104
Pb	SIG	SIG	SIG	SIG	N.S.
SO ₂	SIG	N.S.	N.S.	N.S.	SIG
Interaction	SIG	N.S.	N.S.	N.S.	N.S.

Table 28 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for total serum potassium (K-mEq/liter) for male and female monkeys in Statistica Grouping C.

Groups	Time-Weeks			
	Pre-exposure -8	4	16	68
I - Control	3.75 (0.24)	3.67 (0.20)	3.64 (0.21)	4.02 (0.10)
II - 9.70 ppm SO ₂	4.02 (0.24)	4.10 (0.21)	4.48 (0.40)	4.01 (0.07)
III - 0.51 mg/m ³ PbClBr	3.62 (0.09)	3.76 (0.24)	3.86 (0.18)	3.86 (0.15)
IV - 9.93 ppm SO ₂ + 0.50 mg/m ³ PbClBr	4.41 (0.22)	4.26 (0.12)	3.69 (0.05)	4.04 (0.24)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks			
	Pre-exposure -8	4	16	68
Pb	N.S.	N.S.	N.S.	N.S.
SO ₂	SIG	SIG	N.S.	N.S.
Interaction	N.S.	N.S.	N.S.	N.S.

Table 29 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for total serum chlorides (Cl - mEq/liter) for male and female monkeys in Statistical Grouping C.

Groups	Time-Weeks					
	Pre-exposure	-8	4	16	68	104
I - Control	112.0 (1.1)		109.7 (0.6)	108.4 (1.0)	110.2 (0.8)	112.8 (1.3)
II - 9.70 ppm SO ₂	112.7 (0.6)		111.0 (0.6)	104.0 (0.4)	107.6 (0.5)	108.3 (0.4)
III - 0.51 mg/m ³ PbClBr	112.9 (0.5)		103.2 (0.4)	109.9 (0.6)	111.5 (0.8)	112.3 (0.4)
IV - 9.93 ppm SO ₂ + 0.50 ng/m ³ PbClBr	101.2 (1.1)		106.5 (0.4)	109.0 (0.6)	110.4 (0.8)	113.9 (0.5)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks					
	Pre-exposure	-8	4	16	68	104
pb	SIG		SIG	SIG	SIG	SIG
	SIG		SIG	SIG	SIG	N.S.
Interaction	SIG		N.S.	SIG	N.S.	SIG

Table 30 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for total serum carbon dioxide (CO_2 - mEq/liter) for male and female monkeys in Statistical Grouping C.

Groups	Time-Weeks			
	Pre-exposure -8	4	16	104
I - Control	24.8 (1.0)	24.3 (0.8)	28.9 (0.7)	26.4 (0.7)
II - 9.70 ppm SO_2	27.3 (0.4)	28.2 (0.4)	28.5 (0.4)	28.2 (0.5)
III - 0.51 mg/ m^3 PbClBr	26.7 (0.6)	25.7 (0.9)	22.9 (1.7)	24.6 (1.4)
IV - 9.93 ppm SO_2 + 0.50 mg/ m^3 PbClBr	28.2 (1.1)	22.5 (0.5)	23.4 (0.7)	26.6 (0.7)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks			
	Pre-exposure -8	4	16	104
Pb	N.S.	SIG	SIG	N.S.
SO_2	SIG	N.S.	N.S.	SIG
Interaction	N.S.	SIG	N.S.	N.S.

Table 31 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for total serum calcium (Ca - mg percent) for male and female monkeys in Statistical Grouping C.

Groups	Time-Weeks			
	Pre-exposure -8	4	16	68
I - Control	9.47 (0.22)	9.36 (0.11)	10.16 (0.08)	9.55 (0.30)
II - 9.70 ppm SO ₂	9.52 (0.18)	9.12 (0.10)	9.63 (0.11)	9.97 (0.10)
III - 0.51 mg/m ³ PbClBr	9.77 (0.13)	9.32 (0.11)	9.35 (0.22)	9.90 (0.12)
IV - 9.93 ppm SO ₂ + 0.50 mg/m ³ PbClBr	9.43 (0.10)	8.89 (0.11)	9.78 (0.24)	9.74 (0.15)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks			
	Pre-exposure -8	4	16	68
Pb	N.S.	N.S.	N.S.	N.S.
SO ₂	N.S.	SIG	N.S.	N.S.
Interaction	N.S.	N.S.	SIG	N.S.

Table 32 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for total serum glutamic oxaloacetic transaminase (SGOT - K units) for male and female monkeys in Statistical Grouping C.

Groups	Time-Weeks				
	Pre-exposure -8	4	16	68	104
I - Control	26.0 (4.8)	45.4 (3.1)	20.2 (0.8)	97.3 (21.3)	47.0 (6.2)
II - 9.70 ppm SO ₂	36.8 (4.5)	32.3 (3.3)	35.8 (6.4)	38.3 (4.7)	22.4 (1.2)
III - 0.51 mg/m ³ PbClBr	30.2 (2.1)	31.6 (2.2)	57.0 (10.7)	53.3 (4.5)	44.6 (5.4)
IV - 9.93 ppm SO ₂ + 0.50 mg/m ³ PbClBr	29.2 (2.0)	43.8 (3.9)	73.5 (15.2)	104.4 (23.5)	56.4 (3.0)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks				
	Pre-exposure -8	4	16	68	104
Pb	N.S.	N.S.	SIG	N.S.	SIG
SO ₂	N.S.	N.S.	N.S.	N.S.	N.S.
Interaction	N.S.	SIG	N.S.	SIG	SIG

Table 33 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for total serum glutamic pyruvic transaminase (SGPT - RF units) for male and female monkeys in Statistical Grouping C.

Groups	Time-Weeks			
	Pre-exposure -8	4	16	68
I - Control	15.4 (2.8)	20.7 (3.0)	25.1 (2.7)	41.4 (2.8)
II - 9.70 ppm SO ₂	27.2 (9.2)	33.1 (6.0)	23.9 (1.4)	31.8 (2.2)
III - 0.51 mg/m ³ PbClBr	26.3 (2.5)	27.7 (1.5)	20.2 (3.0)	42.6 (8.1)
IV - 9.93 ppm SO ₂ + 0.50 mg/m ³ PbClBr	33.5 (1.6)	30.4 (2.1)	31.4 (2.5)	32.8 (1.7)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks			
	Pre-exposure -8	4	16	68
Pb	N.S.	N.S.	N.S.	N.S.
SO ₂	N.S.	SIG	N.S.	SIG
Interaction	N.S.	N.S.	SIG	SIG

Table 34 -- Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for total lactic acid dehydrogenase (LDH - WROB units) for male and female monkeys in Statistical Grouping C.

Groups	Pre-exposure -8	Time-Weeks			104
		4	16	68	
I - Control	512 (99)	746 (48)	572 (80)	1573 (156)	597 (93)
II - 9.70 ppm SO ₂	1088 (302)	757 (85)	826 (113)	799 (81)	547 (58)
III - 0.51 mg/m ³ PbClBr	926 (56)	794 (82)	822 (173)	1306 (129)	440 (41)
IV - 9.93 ppm SO ₂ + 0.50 mg/m ³ PbClBr	787 (63)	824 (76)	1102 (187)	1342 (144)	824 (123)

Comparison of Experimental Treatment Effects ($p < .05$)

Source of Variation	Pre-exposure -8	Time-Weeks			104
		4	16	68	
Pb	N.S.	N.S.	N.S.	N.S.	N.S.
SO ₂	N.S.	N.S.	N.S.	SIG	N.S.
Interaction	SIG	N.S.	N.S.	SIG	SIG

Table 35 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for total alkaline phosphatase (Alk. P04 - KA units) for male and female monkeys in Statistical Grouping C.

Groups	Time-Weeks					
	Pre-exposure	-8	4	16	68	104
I - Control	57.2 (17.3)	58.6 (8.8)	55.3 (8.3)	41.9 (7.3)	48.4 (8.6)	
II - 9.70 ppm SO ₂	91.6 (48.3)	40.0 (4.1)	50.5 (9.7)	53.8 (8.1)	41.2 (7.2)	
III - 0.51 mg/m ³ PbClBr	54.4 (8.6)	50.7 (6.9)	67.5 (9.9)	49.2 (8.4)	41.4 (7.6)	
IV - 9.93 ppm SO ₂ + 0.50 mg/m ³ PbClBr	41.4 (4.2)	52.0 (11.2)	61.1 (9.1)	55.9 (9.0)	49.9 (11.2)	

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks					
	Pre-exposure	-8	4	16	68	104
Pb	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.
SO ₂	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.
Interaction	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.

Table 36 - Mean values $\pm$ (S.E.) for blood gas and pH variables measured in male and female monkeys in Statistical Grouping C, comprised of the following: Group I - Control, Group II - 9.70 ppm SO₂, Group III - 0.51 mg/m³ PbClBr, and Group IV - 9.93 ppm SO₂ + 0.50 mg/m³ PbClBr.

Interval Week	PO ₂				PCO ₂				pH			
	Group I	Group II	Group III	Group IV	Group I	Group II	Group III	Group IV	Group I	Group II	Group III	Group IV
-3	91.6 (2.0)	89.5 (0.1)	87.5 (1.7)	86.9 (1.4)	39.9 (0.7)	37.6 (0.6)	41.0 (0.8)	44.2 (1.1)	7.38 (0.00)	7.39 (0.00)	-	7.37 (0.01)
1	87.8 (1.8)	83.4 (1.3)	91.9 (2.7)	85.8 (1.1)	37.2 (1.0)	40.2 (0.5)	43.8 (1.2)	45.2 (1.7)	7.37 (0.00)	7.33 (0.01)	7.35 (0.01)	7.37 (0.00)
6	87.8 (1.9)	82.1 (2.1)	88.9 (1.9)	90.4 (2.7)	44.4 (1.0)	39.7 (1.0)	37.9 (1.1)	41.1 (1.4)	-	7.39 (0.00)	7.37 (0.00)	7.36 (0.01)
13	87.5 (0.9)	87.1 (2.5)	90.5 (1.3)	85.0 (1.8)	39.8 (1.3)	38.2 (1.2)	38.2 (1.1)	43.8 (1.6)	7.37 (0.00)	7.35 (0.01)	7.37 (0.01)	7.36 (0.00)
26	89.6 (1.9)	84.5 (1.9)	84.5 (1.1)	92.2 (0.9)	40.3 (1.2)	43.7 (1.0)	38.7 (0.6)	38.7 (1.9)	7.38 (0.01)	7.38 (0.00)	7.37 (0.01)	7.39 (0.01)
39	85.8 (1.2)	85.5 (1.6)	88.4 (1.1)	88.9 (1.2)	40.4 (1.8)	34.7 (1.1)	37.4 (1.3)	37.3 (1.1)	7.38 (0.00)	7.36 (0.01)	7.35 (0.01)	7.39 (0.00)
65	86.5 (1.6)	86.7 (1.8)	86.5 (1.7)	-	46.1 (1.6)	42.0 (0.9)	47.4 (0.8)	-	7.38 (0.00)	7.41 (0.00)	7.36 (0.00)	-
78	91.6 (1.6)	94.2 (0.9)	97.7 (2.8)	95.1 (2.4)	42.2 (1.4)	46.0 (1.1)	51.9 (1.1)	41.4 (1.0)	7.35 (0.01)	7.39 (0.00)	7.34 (0.01)	7.36 (0.00)
91	98.5 (2.6)	82.5 (2.5)	94.5 (2.4)	95.9 (1.4)	51.1 (2.4)	50.4 (0.7)	49.8 (1.5)	43.3 (1.3)	7.37 (0.01)	7.35 (0.01)	7.39 (0.01)	7.39 (0.01)
104	96.4 (2.2)	87.8 (2.0)	83.7 (1.0)	90.5 (1.7)	39.7 (1.5)	46.8 (1.3)	39.1 (0.9)	41.3 (1.4)	7.36 (0.01)	7.34 (0.01)	7.34 (0.00)	7.37 (0.00)

Table 37 - Mean values $\pm$ (S.D.) and summary of single classification analysis of variance for terminal body weight (g.), organ weight (g.), and organ/body weight ratios (%) for male monkeys for Statistical Grouping C, comprised of the following:
Group I - Control; Group II - 9.70 ppm SO_2 ; Group III - 0.51 mg/ m^3 PbClBr, and Group IV - 9.93 ppm SO_2 + 0.50 mg/ m^3 PbClBr.

Groups	Terminal Body Weight	Brain	Thyroid	Lung	Heart	Liver	Kidneys	Adrenals
		wt. ratio	wt. ratio	wt. ratio	wt. ratio*	wt. ratio	wt. ratio	wt. ratio
I	4920 (1410)	73.8 (7.7)(0.31)	0.53 (0.34)	27.8 (6.0)	16.6 (4.6)(0.05)	88.1 (13.3)(0.25)	18.6 (4.6)(0.05)	0.63 (0.13)(0.002)
II	4700 (829)	64.9 (6.5)(0.24)	0.56 (0.11)	26.6 (3.2)	15.8 (3.2)(0.03)	80.6 (8.3)(0.15)	16.6 (2.4)(0.01)	0.83 (0.03)(0.003)
III	4720 (2252)	67.3 (3.5)(0.45)	0.41 (0.13)	28.2 (9.9)	16.4 (7.4)(0.01)	84.8 (26.5)(0.27)	18.3 (7.6)(0.05)	0.76 (0.35)(0.003)
IV	4580 (1219)	63.4 (5.2)(0.27)	0.51 (0.20)	25.5 (2.9)	15.3 (4.0)(0.01)	97.6 (15.8)(0.39)	20.8 (2.0)(0.07)	0.85 (0.15)(0.004)
Significant Differences ($p \leq .05$)								
I vs II	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	SIG N.S.
I vs III	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.
I vs IV	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	SIG
II vs III	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.
II vs IV	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	SIG	N.S.
III vs IV	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.

* The variances of these groups were heterogeneous.

Table 38 - Mean values $\pm$ (S.D.) and summary of single classification analysis of variance for terminal body weight (g.), organ weight (g.), and organ/body weight ratios (%) for female monkeys for Statistical Grouping C, comprised of the following: Group I - Control, Group II - 9.70 ppm SO₂, Group III - 0.51 mg/m³ PbClBr, and Group IV - 9.93 ppm SO₂ + 0.50 mg/m³ PbClBr.

Groups	Terminal Body Weight	Brain		Thyroid		Lung		Heart		Liver		Kidneys		Adrenals	
		wt.*	ratio	wt.	ratio	wt.	ratio	wt.	ratio	wt.	ratio*	wt.	ratio	wt.*	ratio*
I	3075 (206)	59.5 (3.1)	1.94 (0.13)	0.43 (0.09)	0.014 (0.004)	21.5 (2.4)	0.70 (0.08)	9.7 (0.8)	0.31 (0.01)	66.3 (4.4)	2.16 (0.17)	13.2 (1.4)	0.43 (0.04)	0.76 (0.29)	0.025 (0.010)
II	3325 (624)	60.9 (2.8)	1.87 (0.30)	0.60 (0.08)	0.018 (0.004)	23.6 (1.1)	0.72 (0.11)	10.2 (1.5)	0.31 (0.03)	63.7 (4.8)	1.95 (0.27)	12.7 (1.0)	0.39 (0.05)	0.58 (0.04)	0.018 (0.004)
III	2750 (342)	58.9 (6.3)	2.16 (0.32)	0.30 (0.11)	0.011 (0.004)	20.7 (2.8)	0.75 (0.05)	10.2 (2.7)	0.37 (0.05)	59.0 (9.7)	2.14 (0.14)	13.7 (1.8)	0.50 (0.05)	0.69 (0.13)	0.025 (0.002)
IV	3075 (287)	57.9 (0.9)	1.89 (0.19)	0.35 (0.11)	0.011 (0.004)	18.9 (0.7)	0.62 (0.06)	11.8 (2.7)	0.38 (0.06)	82.0 (7.7)	2.67 (0.04)	14.8 (1.2)	0.48 (0.01)	0.72 (0.09)	0.023 (0.002)
Significant Differences ($p \leq 0.05$)															
I vs II	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.
I vs III	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.
I vs IV	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	SIG	N.S.	N.S.	N.S.	N.S.
II vs III	N.S.	N.S.	N.S.	SIG	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	SIG	N.S.	SIG
II vs IV	N.S.	N.S.	N.S.	SIG	N.S.	SIG	N.S.	N.S.	N.S.	SIG	SIG	N.S.	N.S.	SIG	N.S.
III vs IV	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	SIG	SIG	N.S.	N.S.	N.S.	N.S.

* The variances of these groups were heterogeneous.

Table 39 - Histopathology incidence table for Statistical Grouping C,
 comprised of the following: Group I - Control, Group II - 9.70 ppm
 SO₂, Group III - 0.51 mg/m³ PbClBr, and Group IV - 9.93 ppm SO₂ +
 0.50 mg/m³ PbClBr.

	GROUPS			
	I	II	III	IV
LUNG				
Focal Pleural Thickening	2/9	2/9	2/9	1/9
Peribronchial Brown Pigment	1/9	5/9	3/9	2/9
Artifactual Emphysema	4/9	5/9	0/9	0/9
Alveolar Duct Fibrosis	9/9	3/9	2/9	2/9
Thickening Bronchiolar Wall	0/9	0/9	1/9	0/9
Bronchiolar Epithelial Hyperplasia	0/9	0/9	1/9	0/9
Bronchiolar Epithelial Hypertrophy	0/9	0/9	2/9	0/9
Pneumonocyte Hyperplasia	1/9	1/9	0/9	2/9
Peribronchial Lymphoid Hyperplasia	1/9	0/9	0/9	2/9
Emphysema	0/9	0/9	0/9	1/9
Focal Necrosis	0/9	1/9	0/9	0/9
Focal Hemorrhage	0/9	1/9	0/9	0/9
Parasite	0/9	1/9	0/9	0/9
Perivascular Edema	0/9	0/9	0/9	0/9
Pulmonary Edema	0/9	1/9	0/9	0/9
Bronchiolitis	1/9	0/9	0/9	1/9
Bronchitis	0/9	0/9	1/9	0/9
Monkey Pox	0/9	1/9	0/9	0/9
Vasculitis	1/9	0/9	0/9	0/9
Granuloma	0/9	0/9	0/9	0/9
Pneumonitis	0/9	0/9	0/9	0/9
Abscess	0/9	0/9	0/9	1/9
Lung Mite Infestation	1/9	0/9	0/9	0/9
Adenomatosis	0/9	0/9	0/9	0/9
Bronchiectasis	0/9	0/9	0/9	0/9
Purulent Pneumonia	0/9	0/9	0/9	0/9
Epithelial Necrosis	0/9	0/9	0/9	0/9
Thickened Alveolar Wall	0/9	0/9	1/9	0/9
Pleuritis	0/9	0/9	0/9	0/9
Crystallin Material (yellow)	0/9	0/9	2/9	1/9
Mucous	0/9	0/9	0/9	2/9
Focal Fibrosis	0/9	0/9	0/9	0/9
Pleural Fibrosis	0/9	0/9	0/9	0/9
Alveolar Wall Fibrosis	0/9	0/9	2/9	2/9
Vacuolated Media	0/9	0/9	0/9	0/9
Endothelial Hyperplasia	0/9	0/9	0/9	0/9
Stenotic	0/9	0/9	0/9	0/9
Chronic Pneumonia	0/9	0/9	0/9	0/9
Eroded Bronchi	0/9	0/9	0/9	0/9
Emphysematous Bulla	0/9	0/9	0/9	0/9

Table 39 - Continued

	GROUPS			
	I	II	III	IV
LUNG - Continued				
Atelectasis	0/9	0/9	0/9	3/9
Congested	0/9	0/9	0/9	0/9
Extravasated Blood	0/9	0/9	0/9	0/9
Collapsed Alveolar Wall	0/9	0/9	0/9	0/9
LIVER				
Pericholangitis	0/9	1/9	3/9	4/9
Bile Duct Proliferation	1/9	3/9	3/9	3/9
Focal Necrosis	0/9	1/9	0/9	0/9
Sinusoidal Pigment	2/9	7/9	2/9	0/9
Focal Hepatitis	0/9	0/9	0/9	0/9
Focal Lymphoid Infiltration	1/9	2/9	1/9	0/9
Nematodiasis	0/9	1/9	0/9	0/9
Thick Capsule	0/9	0/9	0/9	0/9
Granuloma	0/9	0/9	0/9	0/9
Abscess	0/9	0/9	0/9	0/9
Hepatocyte Vacuolation	0/9	0/9	1/9	1/9
Greenish Granular Material in the Hepatocytes	0/9	0/9	1/9	0/9
PERIBRONCHIAL LYMPH NODE				
Phagocytized Pigment	6/9	5/9	7/9	7/9
Lymphoid Activity	8/9	6/9	0/9	0/9
Lymphoid Atrophy	0/9	0/9	0/9	0/9
Adenitis	0/9	0/9	0/9	0/9
Granuloma	1/9	2/9	0/9	0/9
Reticuloendothelial Cell Hyperplasia	1/9	0/9	0/9	0/9
Lymphadenitis	0/9	0/9	0/9	0/9
TRACHEA				
Tracheitis	1/9	0/9	0/9	0/9
Increase in Goblet Cells	0/9	4/9	0/9	0/9
Exudate in Lumen	0/9	1/9	0/9	0/9
Necrosis of the Epithelium	0/9	1/9	0/9	0/9
Inclusion Bodies	0/9	1/9	0/9	0/9
Epithelial Hyperplasia	0/9	1/9	0/9	0/9
Cilia Atrophy	0/9	0/9	0/9	0/9
Squamous Metaplasia	0/9	0/9	0/9	0/9
Focal Hemorrhage	0/9	0/9	0/9	0/9

Table 39 - Continued

	GROUPS			
	<u>I</u>	<u>II</u>	<u>III</u>	<u>IV</u>
KIDNEY				
Interstitial Nephritis	0/9	2/9	2/9	0/9
Epithelial Vacuolation	1/9	3/9	3/9	8/9
Tubular Dilatation	3/9	2/9	0/9	1/9
Loss of the Brush Border	0/9	2/9	3/9	3/9
Nuclear Vesiculation	0/9	0/9	0/9	7/9
Tubular Hypertrophy	0/9	0/9	0/9	1/9
Pyelitis	0/9	1/9	0/9	0/9
Focal Mineralization	0/9	0/9	1/9	0/9
Glomerular Degeneration	0/9	2/9	0/9	0/9
Inclusion Bodies	0/9	0/9	7/9	8/9
Vasculitis	0/9	0/9	0/9	0/9
Congestion	0/9	0/9	0/9	0/9
Focal Fibrosis	0/9	0/9	0/9	0/9
Perirenal Abscess	0/9	0/9	0/9	1/9
Protein Inhibition	0/9	0/9	1/9	0/9
Intima Thickening	0/9	0/9	0/9	0/9
Endothelial Hyperplasia	0/9	0/9	0/9	0/9
HEART				
Focal Myocarditis	3/9	2/9	0/9	0/9
Endocarditis	0/9	0/9	0/9	0/9
Epicarditis	0/9	1/9	0/9	0/9
Myocardial Degeneration	1/9	0/9	0/9	0/9
Vasculitis	0/9	0/9	0/9	0/9
Subendocardial Hemorrhage	0/9	1/9	0/9	0/9
Thickened Endocardium	0/9	0/9	0/9	0/9
Focal Hyperplasia in the Endothelium	0/9	0/9	0/9	0/9
Intima Thickening	0/9	0/9	0/9	0/9
Granular Pigment	0/9	0/9	0/9	0/9



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VI. STATISTICAL GROUPING D - RESULTS OF THE CHRONIC EXPOSURE OF CYNOMOLGUS MONKEYS TO 65.46 PPM CARBON MONOXIDE (CO), 0.51 MG/M³ LEAD CHLOROBROMIDE (PbClBr) AND 66.43 PPM CO COMBINED WITH 0.47 MG/M³ PbClBr.

Four groups of animals comprise the fourth statistical grouping-D. One group was maintained as the control group exposed to filtered room air, while the other three groups were exposed to carbon monoxide and lead chlorobromide singly and in binary combination. Group designations used throughout this section are presented in Table 13.

Table 13 - Group D designations

<u>Group Designation (No.)</u>	<u>Agent</u>	<u>Nominal Concentration</u>	<u>Mean Analytical Concentration</u>
I (1)	Control	0	0
II (7)	CO	67.50 ppm	65.46 ppm
III (9)	PbClBr	0.60 mg/m ³	0.51 mg/m ³
IV (20)	CO	67.50 ppm	66.43 ppm
	PbClBr	0.60 mg/m ³	0.47 mg/m ³

1. Exposure Concentrations

The chamber concentrations as determined analytically are presented in Tables 1, 2, and 3, Appendix D, for Groups II, III, and IV, respectively. The mean and standard deviation for the group exposed to CO alone was 65.46 ppm $\pm$ 3.33; for the group exposed to PbClBr alone 0.51 mg/m³ $\pm$ 0.27; and for the group exposed to the combination of CO and PbClBr, the means and standard deviations were 66.43 ppm $\pm$ 2.28 and 0.47 mg/m³ $\pm$ 0.21, respectively.



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2. Particle Size Determination

The mean and geometric deviation of all count particle size determinations for PbClBr converted to mass median diameter (MMD) were $0.550\mu \pm 1.57$ and $1.050\mu \pm 1.79$ for Groups III and IV, respectively. A composite size vs. distribution log-probability plot from the pooled count data is presented in Figures 66 and 67 for Groups III and IV, respectively.

3. Biological Measurements

3.1. Body Weight

Analysis of variance of regression for body weight (Table 4, Appendix D) indicated no significant differences in slopes among the groups. The regression curves (Figure 68) indicated a trend toward increasing body weight values in all groups and growth rate was similar in all groups except Group II which started slightly heavier and ended slightly lighter due to the deaths of two male members of the group.

3.2. Survival

No deaths occurred in Groups I, III or IV during the 104 weeks of exposure. Two deaths occurred in Group II during Weeks 42 and 78 of the exposure period. Daily observation of the animals revealed no clinical signs of toxicity or abnormal behavior attributable to the exposure atmospheres.

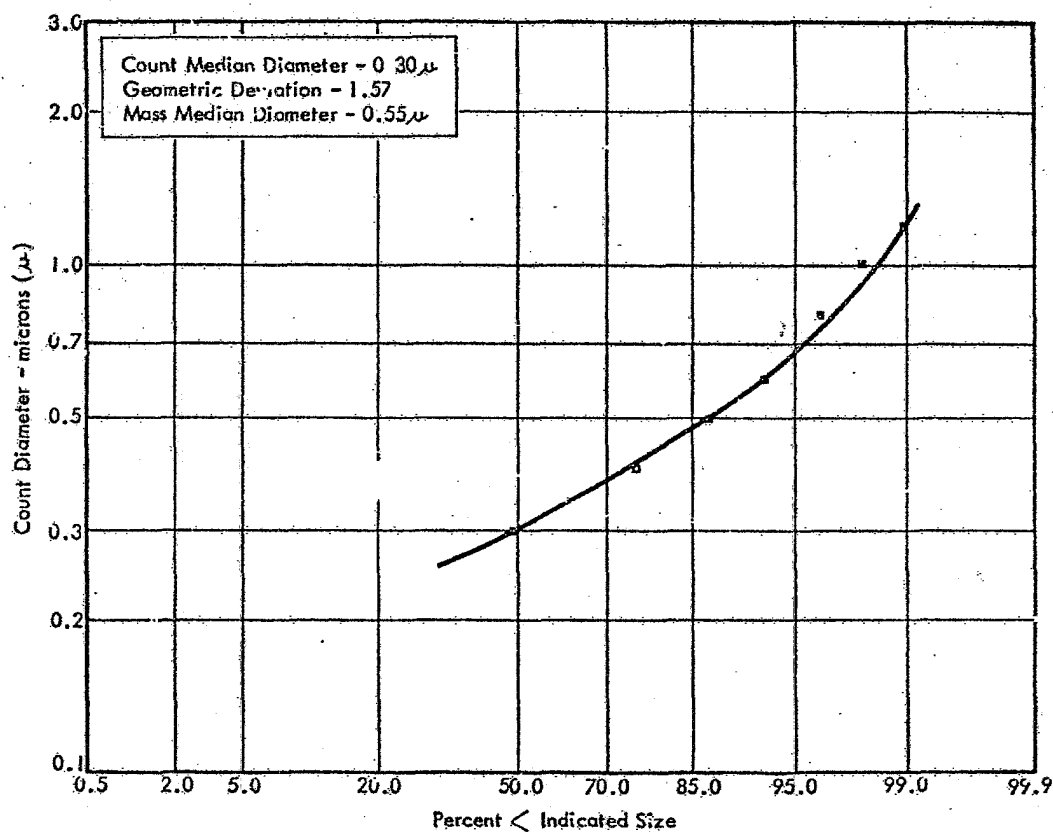


Figure 66 - Particle size distributions (count diameter) of PbClBr .

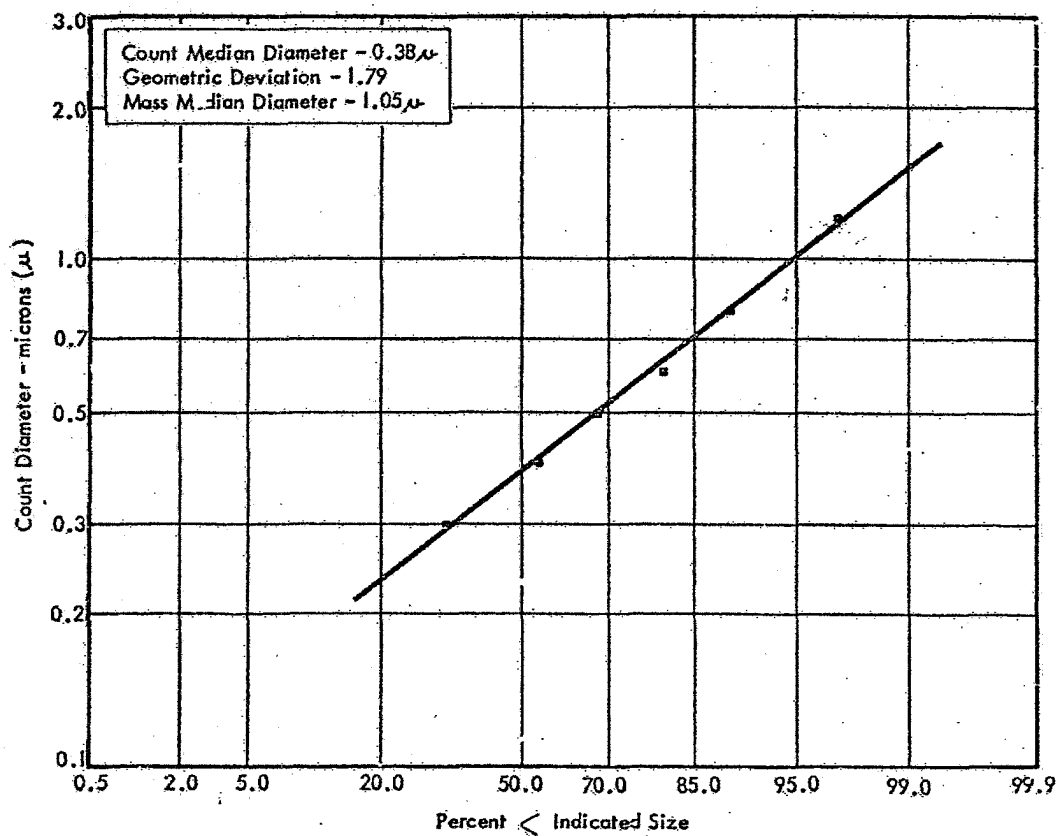


Figure 67 - Particle size distributions (count diameter) of PbClBr for the group exposed to the combination of PbClBr and CO.

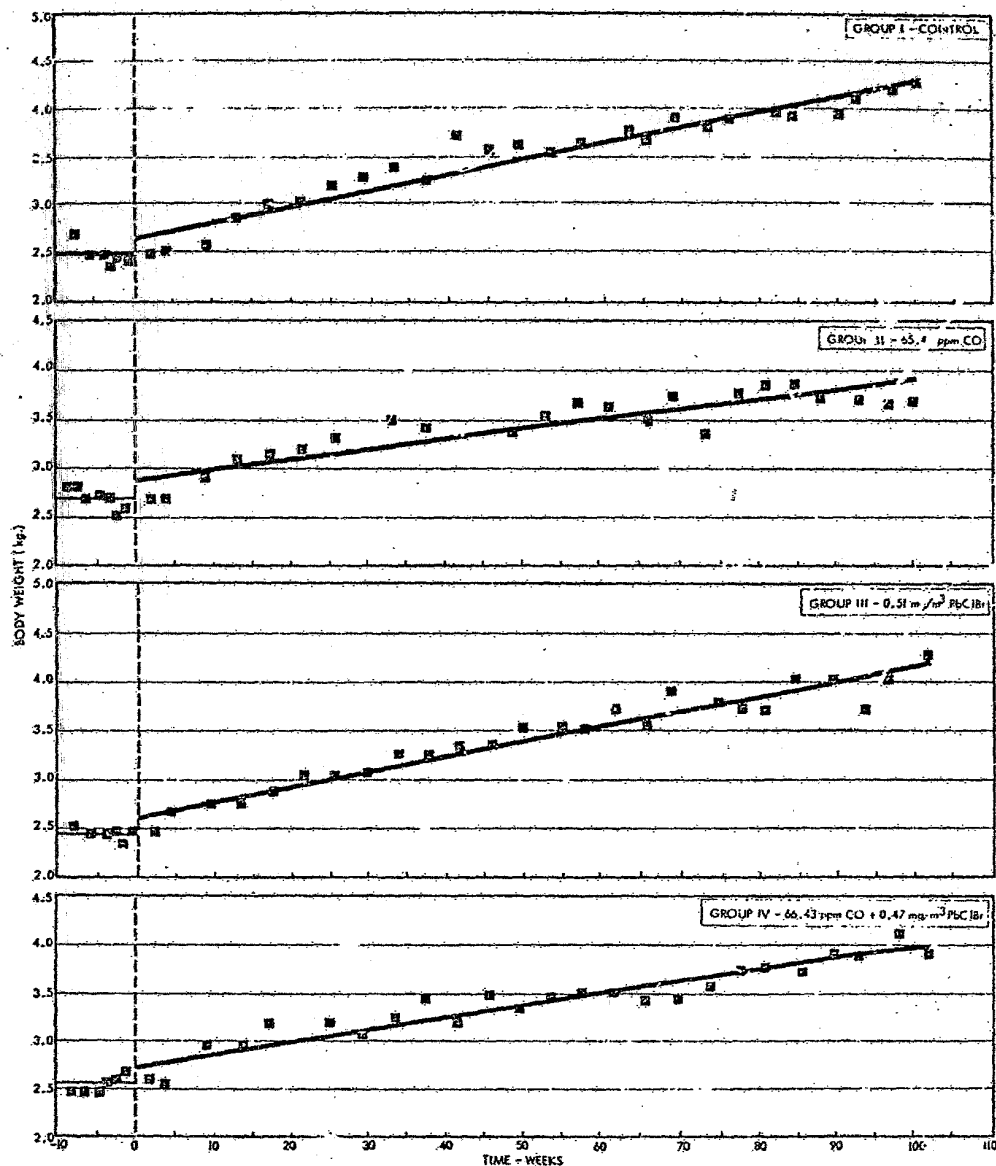


Figure 68 - First degree polynomial regression curves for body weight prior to and during exposure to carbon monoxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.



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3.3. Pulmonary Function Tests

3.3.1. Mechanical Properties of the Lung and Respiratory System

3.3.1.1. Total Respiratory System Flow Resistance During Inspiration [$R_{rs(i)}$]

Analysis of variance of regression for $R_{rs(i)}$ (Table 5, Appendix D) revealed non-parallelism among the groups. The third degree polynomial regression curves (Figure 69) indicated that $R_{rs(i)}$ values for Group I decreased slightly at the beginning of the exposure whereas values for Groups III and IV similarly increased slightly. Separate t-tests of the pre-exposure adjusted means for the first nine weeks indicated that Group I was significantly lower than Group III and Group IV during this early interval ($t = 4.33$, d.f. = 16 and $t = 4.66$, d.f. = 16, respectively).

3.3.1.2. Total Respiratory System Flow Resistance During Expiration [$R_{rs(e)}$]

Analysis of variance of regression for $R_{rs(e)}$ (Table 6, Appendix D) indicated non-parallelism among the groups. Third degree polynomial regression curves (Figure 70) indicated that Group II started into the experiment with lower $R_{rs(e)}$ values than the other groups, and did not exhibit as much of a decrease as the other groups. A t-test of pre-exposure adjusted overall exposure means comparing Groups I and II indicated that Group II was relatively significantly higher throughout the exposure period ($t = 5.03$, d.f. = 14.3). A similar test comparing Groups I and IV indicated that Group IV was relatively higher also ($t = 3.72$, d.f. = 16). Group III was not significantly different from Group I by this test ($t = 1.92$, d.f. = 16).

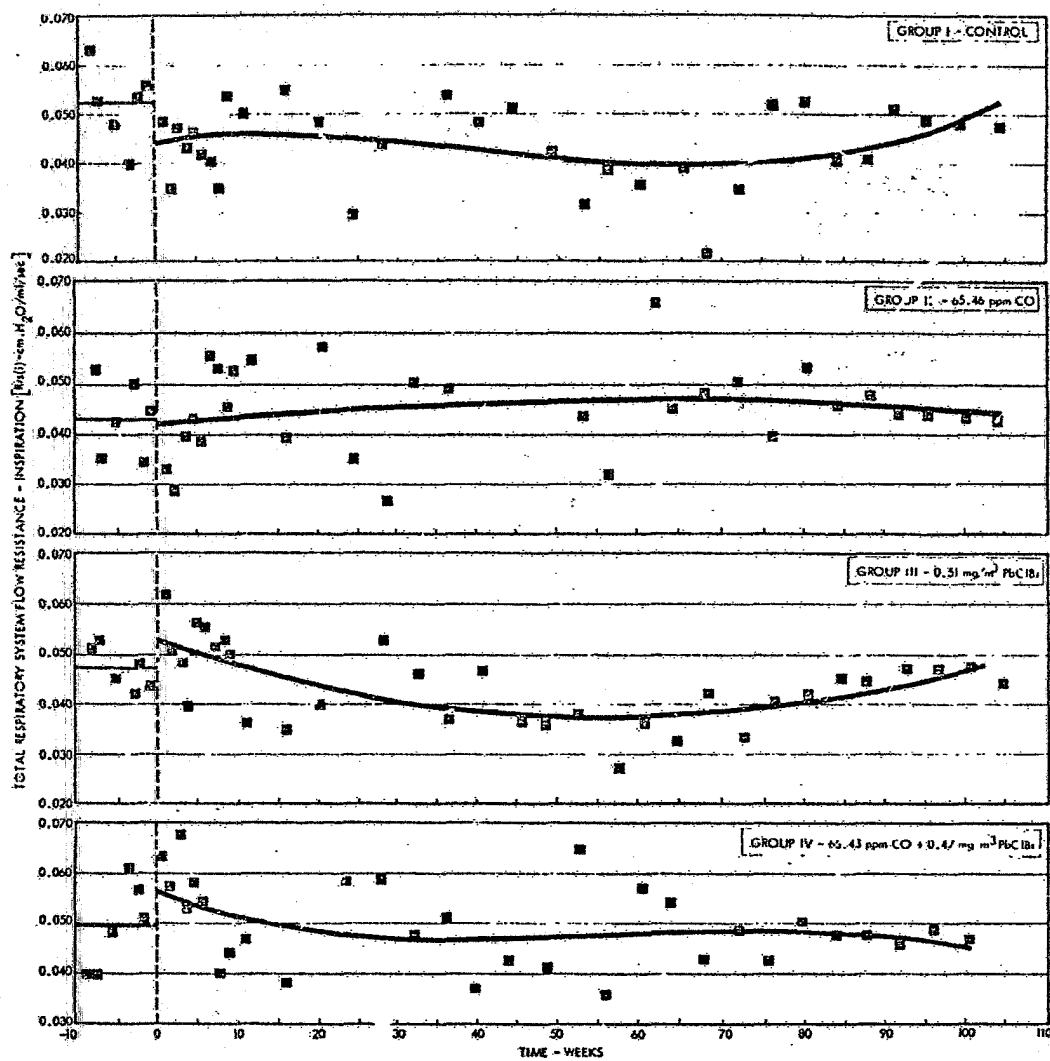


Figure 69 - Third degree polynomial regression curves for $Rrs(i)$ prior to and during exposure to carbon monoxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.

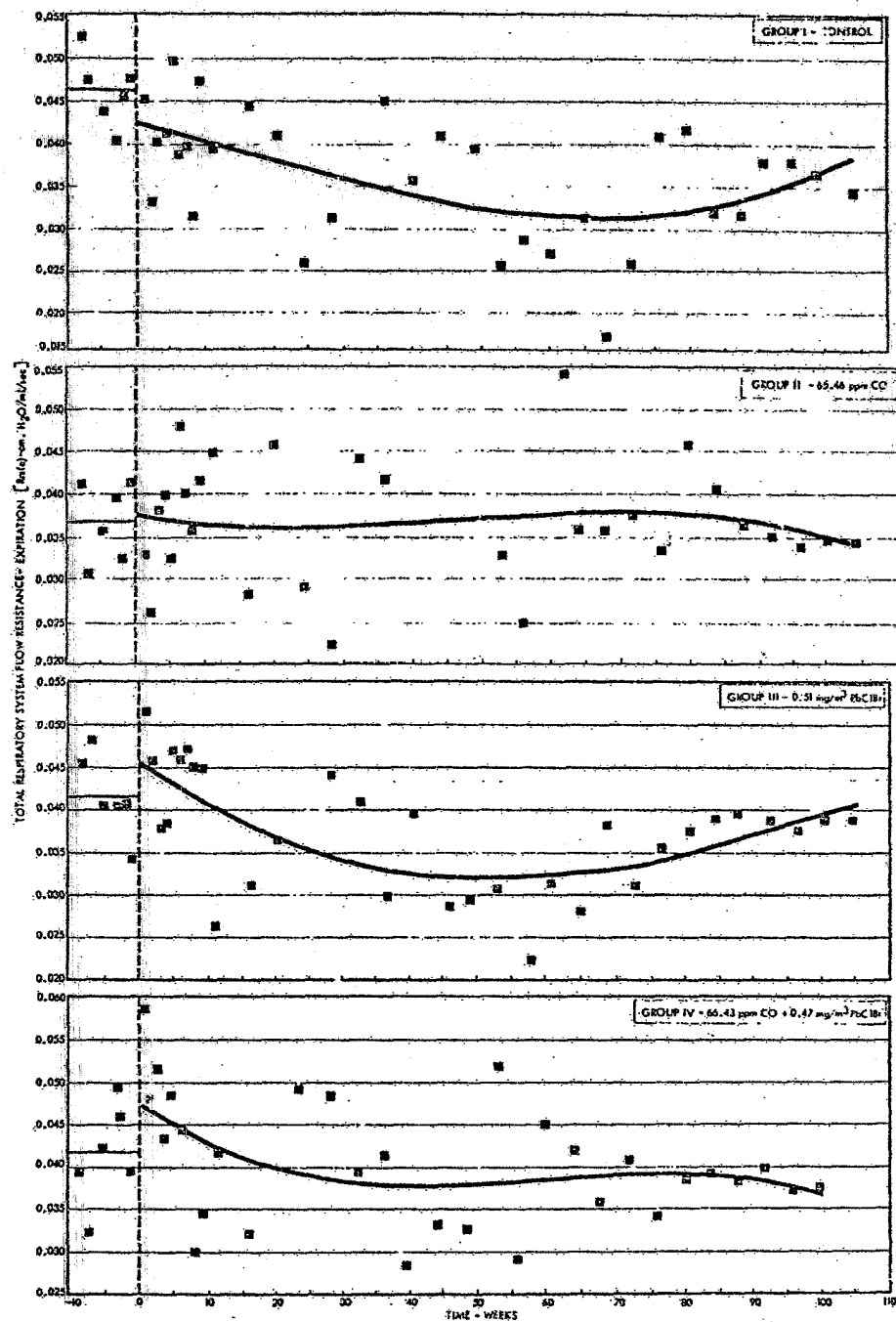


Figure 70 - Third degree polynomial regression curves for $R_{rs}(e)$ prior to and during exposure to carbon monoxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.



3.3.1.3. Tidal Volume (V_T)

Analysis of variance of regression for V_T (Table 7, Appendix D) revealed no significant differences in slopes among the groups. V_T increased with time in all groups, as shown in Figure 71.

3.3.1.4. Respiratory Rate (RR)

Analysis of variance of regression for RR (Table 8, Appendix D) indicated slight non-parallelism among the groups. The third degree polynomial regression curves (Figure 72) indicated that Groups II, III, and IV exhibited essentially no change during the exposure period, while Group I demonstrated slightly decreasing values due to an abrupt increase after "exposure" started.

3.3.1.5. Dynamic Compliance of the Lung [$C_{dyn}(1)$]

Analysis of variance of regression for $C_{dyn}(1)$ (Table 9, Appendix D) revealed no significant differences in slopes among the groups. The third degree polynomial regression curves (Figure 73) indicated that all groups increased in $C_{dyn}(1)$ during the experiment, with Group I showing a sharp increase after "exposure" began. Although the pre-exposure adjusted means of the first year were significantly different between Groups I and III ($t = 2.69$, d.f. = 16), the fact that Group I showed a large increase at the start of exposure renders any interpretation difficult.

3.3.1.6. Pulmonary Flow Resistance (R_I)

Analysis of variance of regression for R_I (Table 10, Appendix D) indicated non-parallelism among the groups. The third degree polynomial regression curves (Figure 74) indicated that Group I did not decrease as much as the other groups during the exposure period. During the first nine weeks

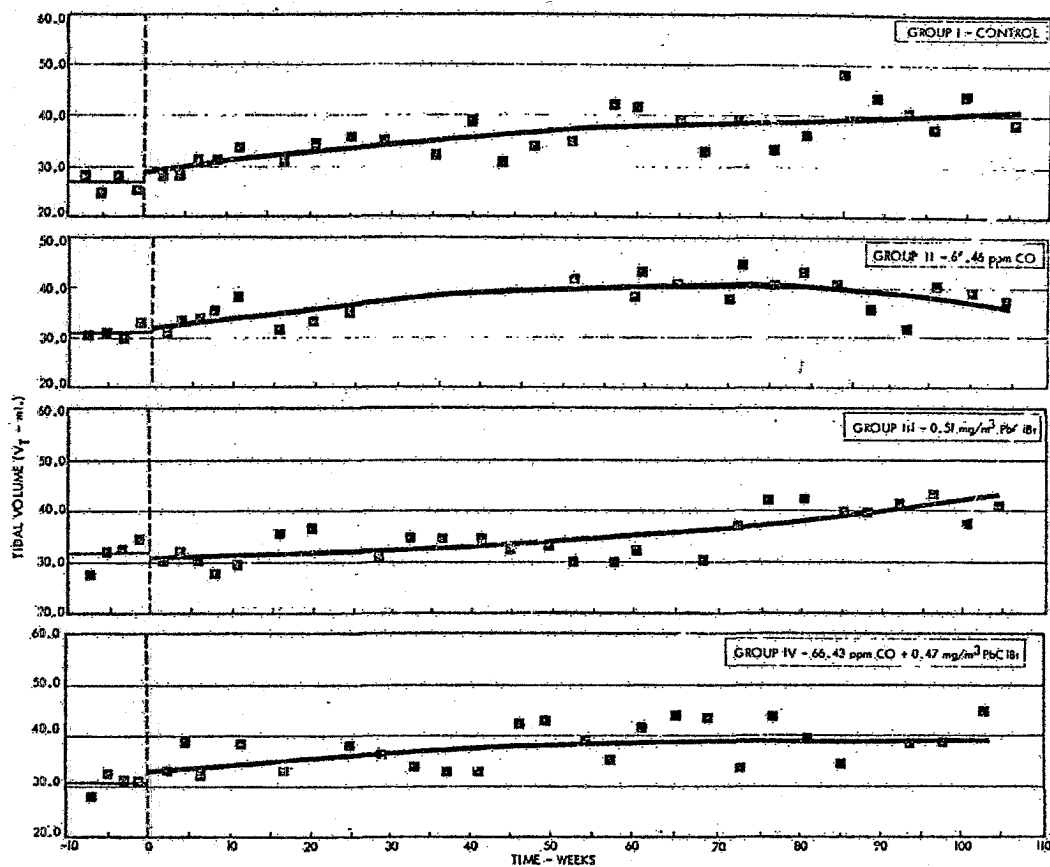


Figure 71 - Third degree polynomial regression curves for V_T prior to and during exposure to carbon monoxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.

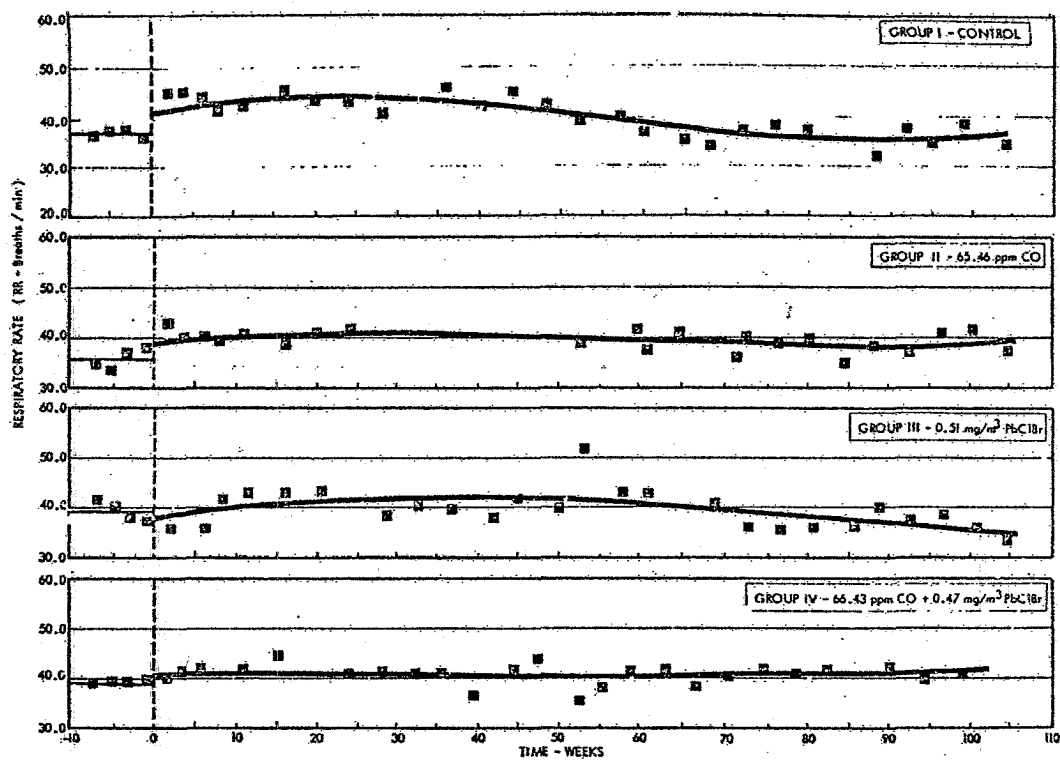


Figure 72 - Third degree polynomial regression curves for RR prior to and during exposure to carbon monoxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.

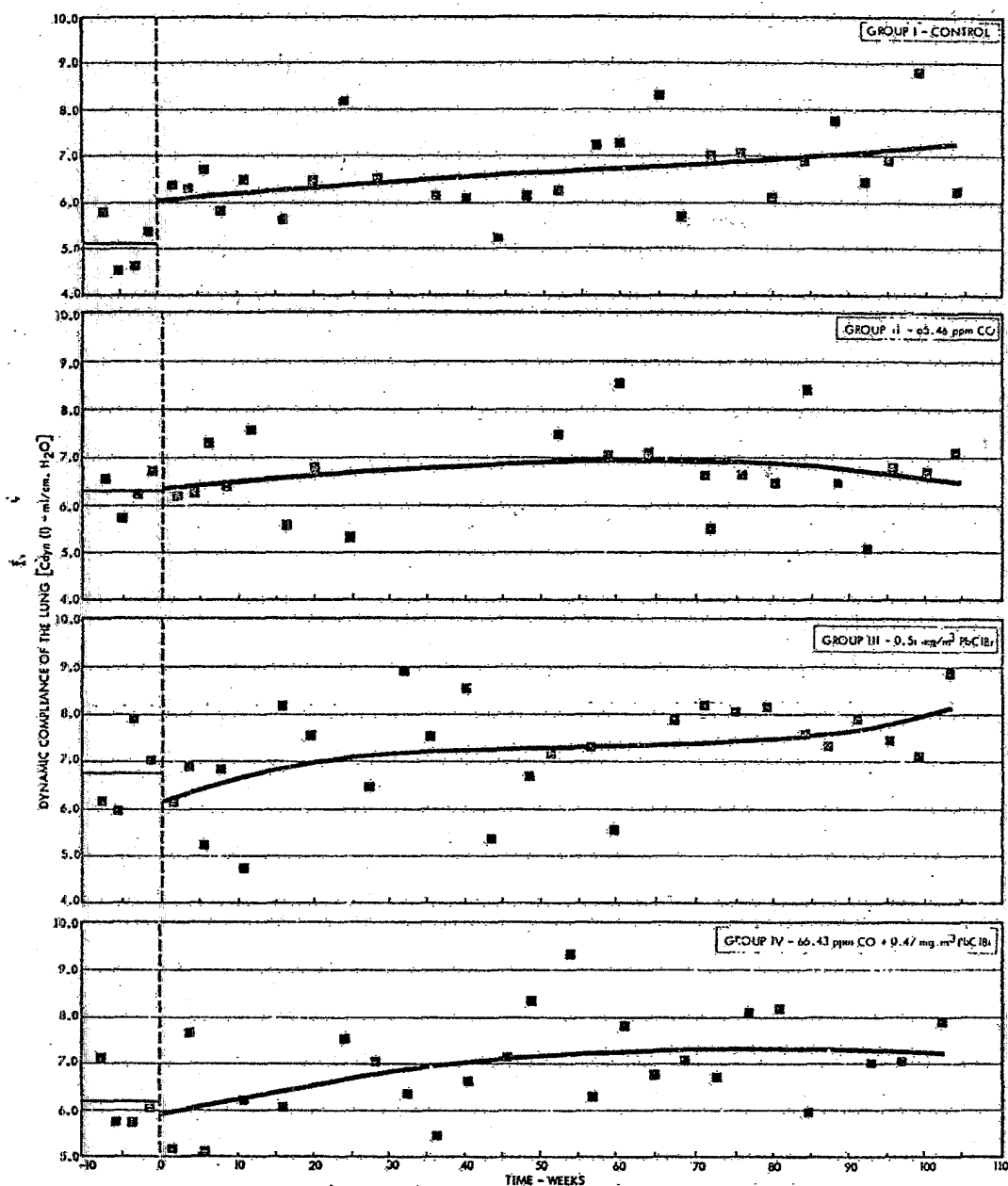


Figure 73 - Third degree polynomial regression curves for $C_{dyn}(1)$ prior to and during exposure to carbon monoxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.

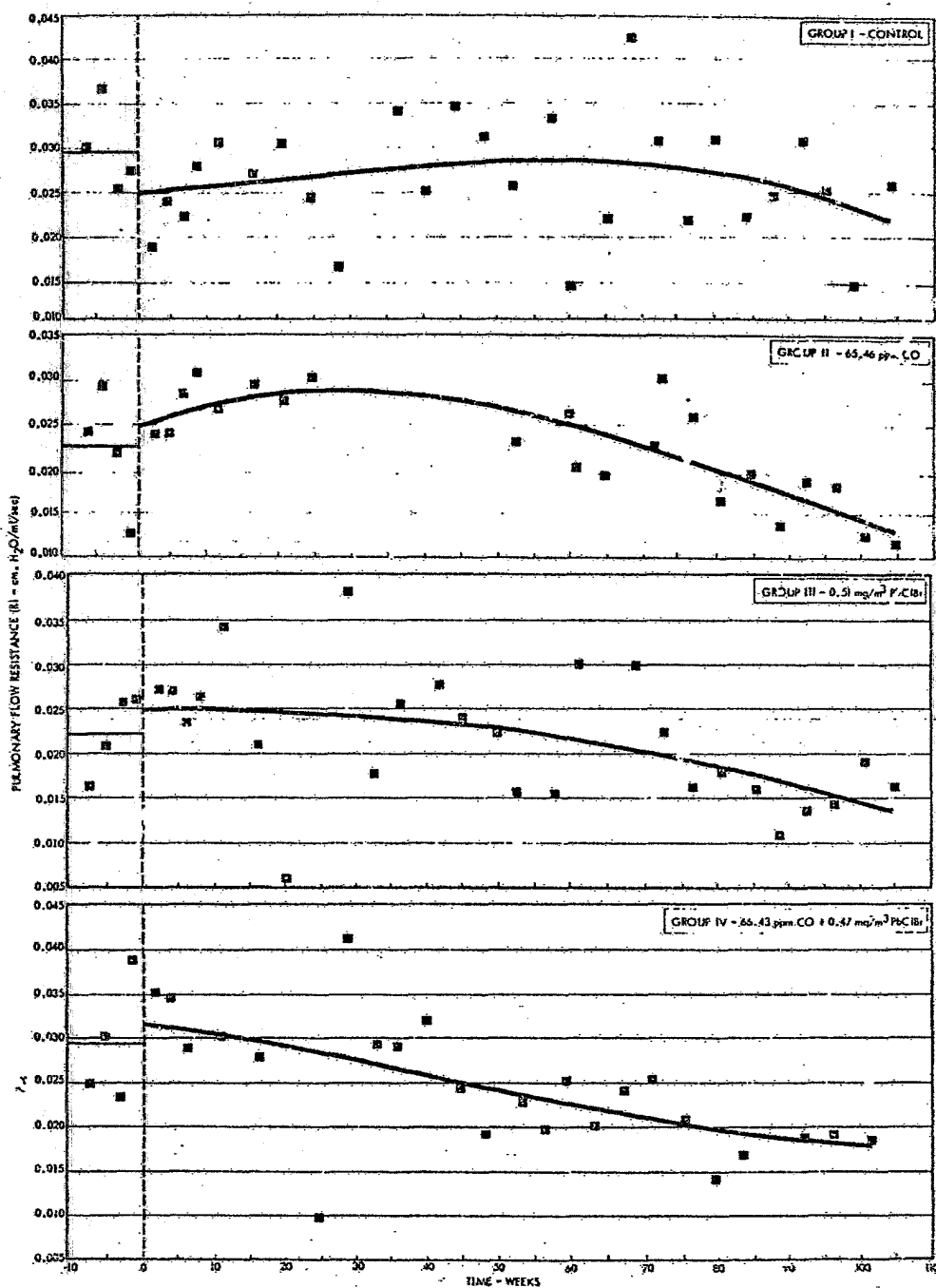


Figure 74 - Third degree polynomial regression curves for Rl prior to and during exposure to carbon monoxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.



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of exposure, Group IV was significantly higher than Group I ($t = 4.66$, d.f. = 16) as was Group III ($t = 2.66$, d.f. = 16). Separate t-tests of the pre-exposure adjusted means of the overall exposure period and of the first 52 weeks exposure between Groups I and II were not significant ($t < 1.64$, d.f. = 16 and $t = 2.05$, d.f. = 16, respectively).

3.3.1.7. Work of Breathing During Inspiration per ml Tidal Volume [$W(i)/ml V_T$]

Analysis of variance of regression for $W(i)/ml V_T$ (Table 11, Appendix D) revealed no significant differences in slopes among the groups. The third degree polynomial regression curves (Figure 75) indicated that Groups III and IV were lower than Group I throughout the exposure period.

3.3.1.8. Work of Breathing During Expiration per ml Tidal Volume [$W(e)/ml V_T$]

Analysis of variance of regression for $W(e)/ml V_T$ (Table 12, Appendix D) indicated no significant differences in slopes among the groups. The third degree polynomial regression curves (Figure 76) indicated very little change in $W(e)/ml V_T$ values throughout the exposure.

3.3.2. Diffusing Capacity of the Lung for Carbon Monoxide (DL_{CO})

Analysis of variance of linear regression for DL_{CO} (Table 13, Appendix D) indicated that there were no significant differences in slopes between the groups. The third degree polynomial regression curves (Figure 77) indicated that all groups increased in DL_{CO} values with time.

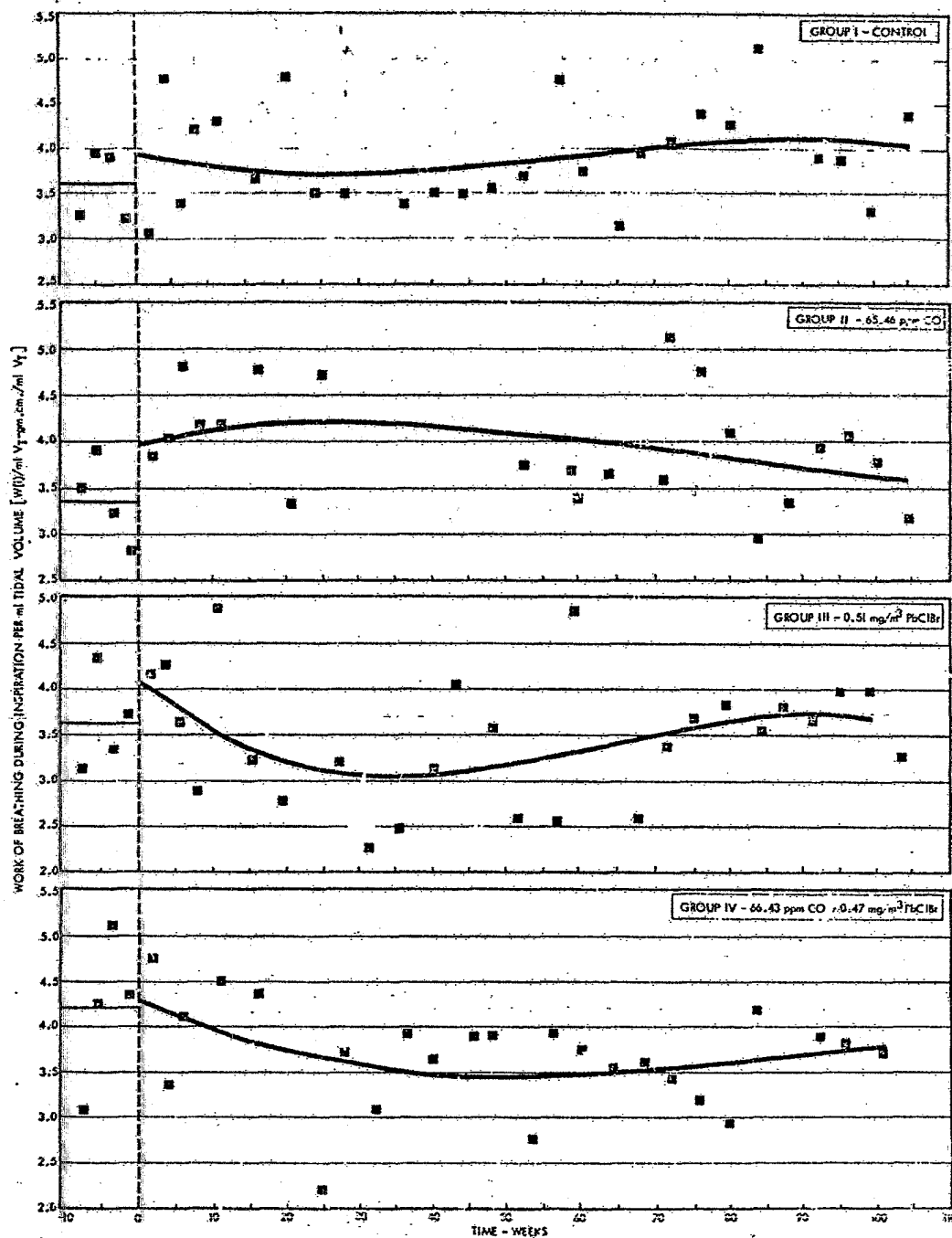


Figure 75 - Third degree polynomial regression curves for $W(i)/ml V_T$ prior to and during exposure to carbon monoxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.

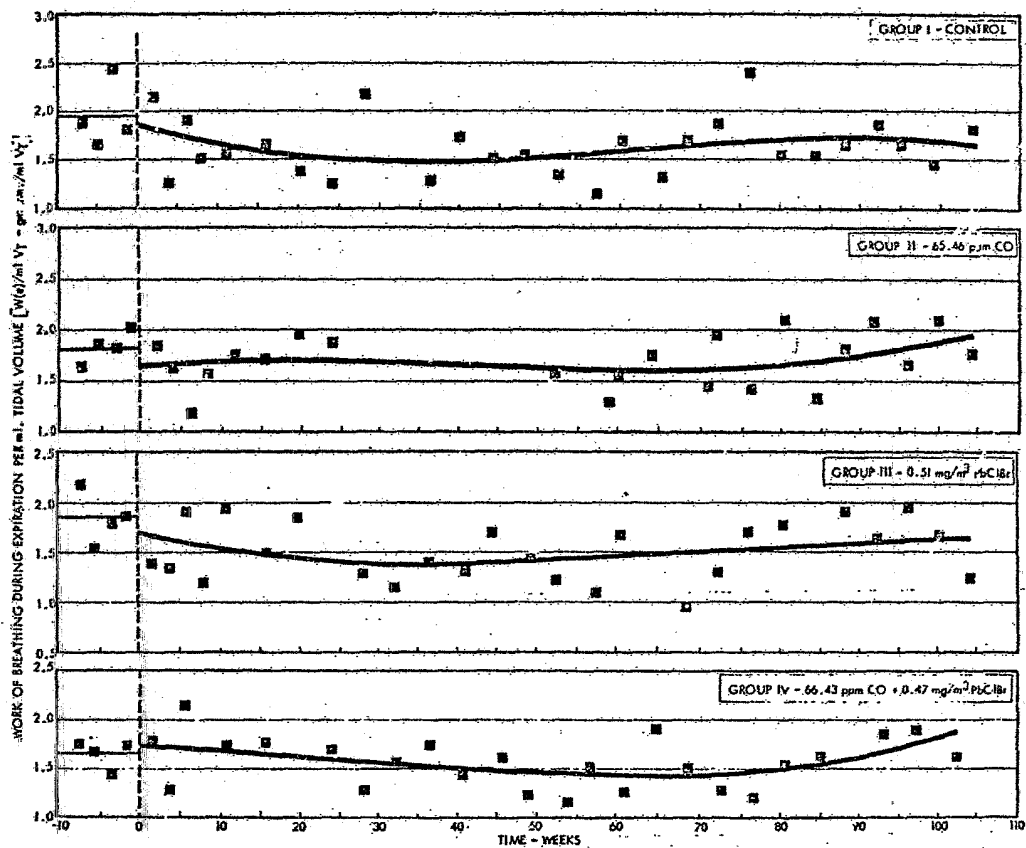


Figure 76 - Third degree polynomial regression curves for $W(e)/ml V_T$ prior to and during exposure to carbon monoxide and lead chlorobromide singly and binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.

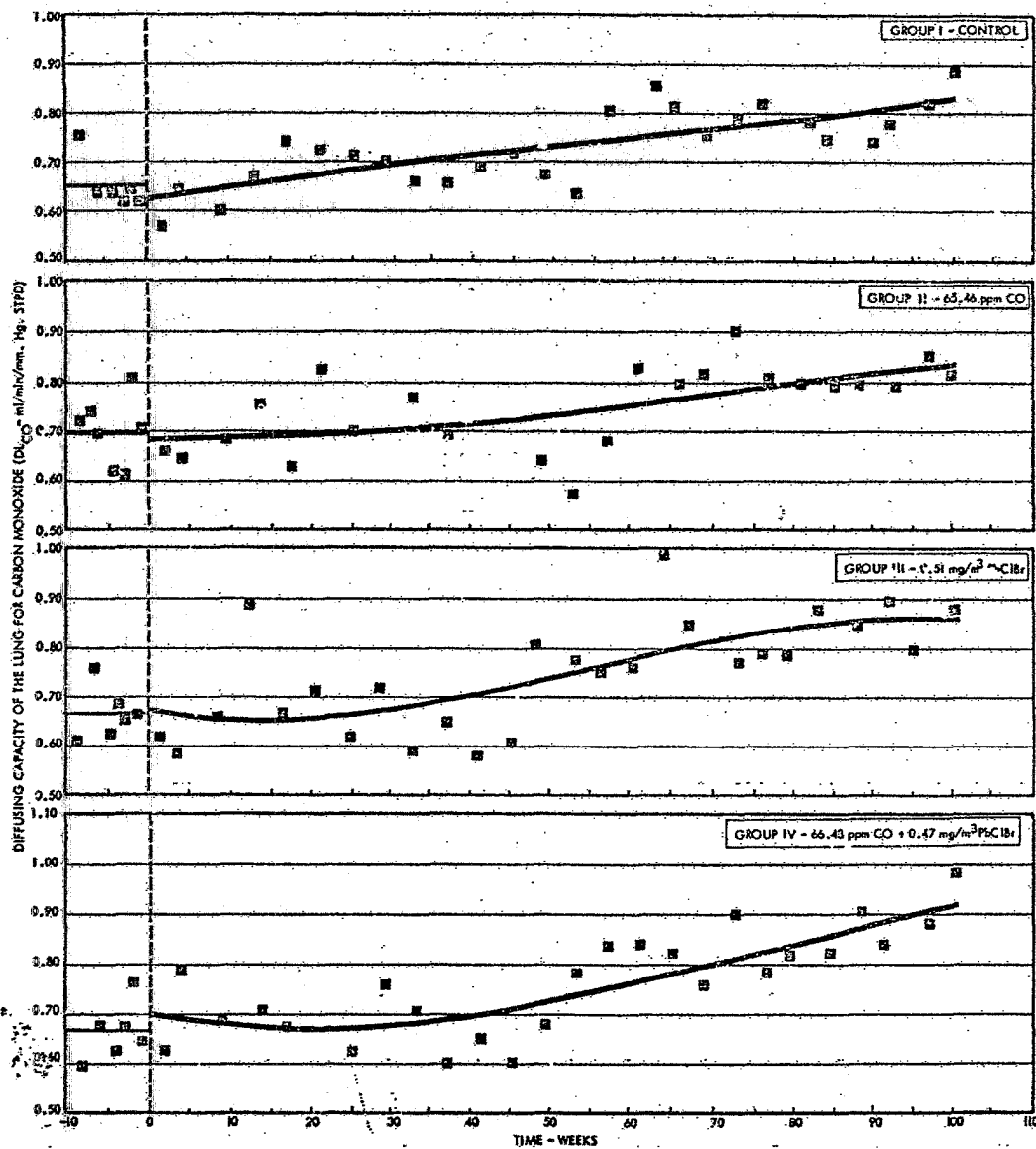


Figure 77 - Third degree polynomial regression curves for DL_{CO} prior to and during exposure to carbon monoxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.



3.3.3. Distribution of Inspired Air, Nitrogen Washout

3.3.3.1. Number of Breaths from 80% to 1% Nitrogen [$N(1\% N_2)$]

Analysis of variance of regression for $N(1\% N_2)$ (Table 14, Appendix D) indicated non-parallelism among the groups. The third degree polynomial regression curves (Figure 78) indicated that values for Group I were somewhat higher during the pre-exposure control period than values for Group II, III, and IV. During the entire exposure period, $N(1\% N_2)$ values for Groups III and IV were at a higher level than Group I values. A t-test of the pre-exposure adjusted overall exposure means of these two groups indicated that Group III was significantly higher than Group I during the exposure period ($t = 4.55$, d.f. = 16). A similar t-test comparing Groups I and IV showed a similar relationship ($t = 5.24$, d.f. = 16). A t-test of the pre-exposure adjusted overall exposure means of Groups I and II showed them to be significantly different ($t = 2.21$, d.f. = 16).

3.3.3.2. Respiratory Rate Measured During Pure Oxygen Breathing (RR')

Analysis of variance of regression for RR' (Table 15, Appendix D) indicated no significant differences in slopes among the groups. The third degree polynomial curves (Figure 79) indicated that Groups II, III, and IV were slightly higher than Group I after the 45th week. Separate t-tests of the pre-exposure adjusted overall exposure means comparing Group I to each of the experimental groups, indicated that the first two groups were relatively higher than Group I throughout exposure ($t = 2.18$, d.f. = 16; $t = 2.61$, d.f. = 16, and $t = 1.64$, d.f. = 16, respectively).

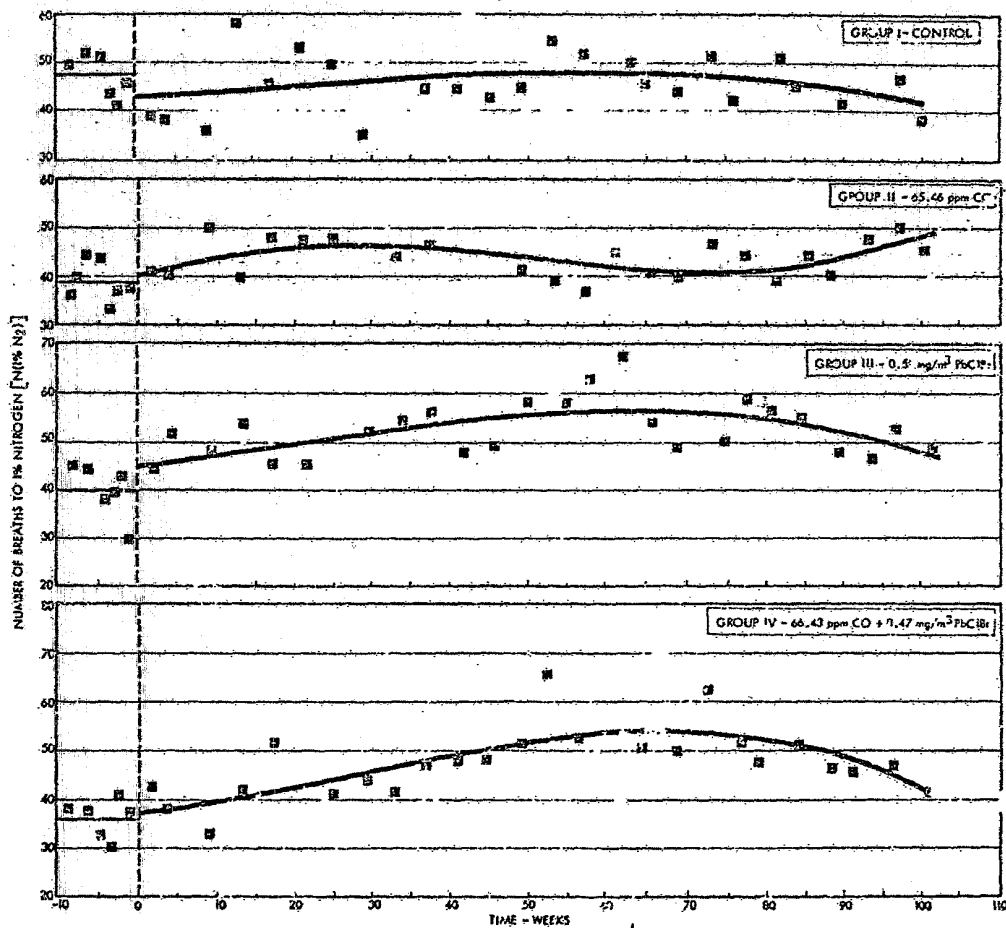


Figure 78 - Third degree polynomial regression curves for N(1% N₂) prior to and during exposure to carbon monoxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.

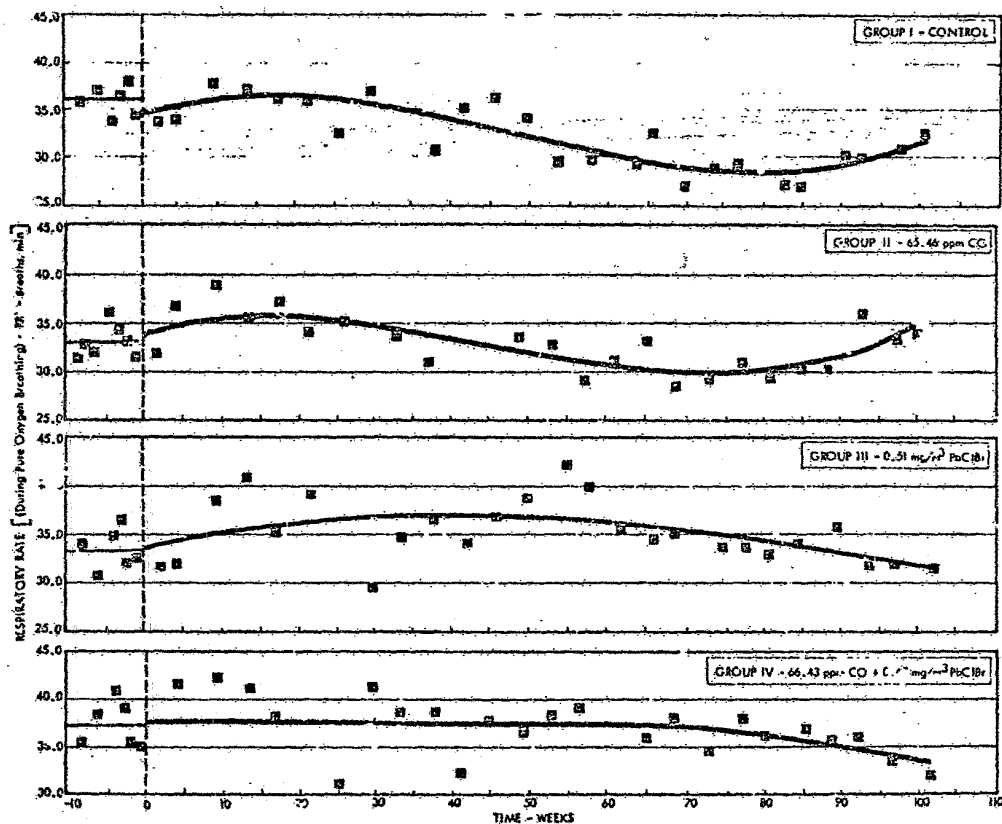


Figure 79 - Third degree polynomial regression curves for RR' prior to and during exposure to carbon monoxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.



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3.3.3.3. Cumulative Tidal Volume from 80% to 1% Nitrogen [$CV_T(1\% N_2)$]

Analysis of variance of regression for $CV_T(1\% N_2)$ (Table 16, Appendix D) indicated non-parallelism among the groups. The third degree polynomial regression curves (Figure 80) indicated that Group III was slightly higher overall than Group I throughout exposure. A t-test of the pre-exposure adjusted overall exposure means comparing these two groups indicated that Group III was significantly higher ($t = 2.24$, d.f. = 13.7) throughout the exposure period.

3.3.3.4. Tidal Volume Measured During Oxygen Breathing (V_T')

Analysis of variance of regression for V_T' (Table 17, Appendix D) revealed non-parallelism among the groups. The third degree polynomial regression curves (Figure 81) indicated that Group I had lower V_T' values than the other groups during the pre-exposure period and exhibited more of an increase during the exposure period. The lack of increase in Group II, when compared to Group I ($t = 2.51$, d.f. = 16), was probably due to the deaths of two males during the exposure period.

3.4. Hematology

The group means and analysis of variances of the various hematological variables measured are presented in Tables 18, 19, 20, and 21, Appendix D. No consistent trends were noted in any of these variables which remained within normal limits throughout. Random statistically significant differences were seen, but were not consistently related to the exposure conditions.

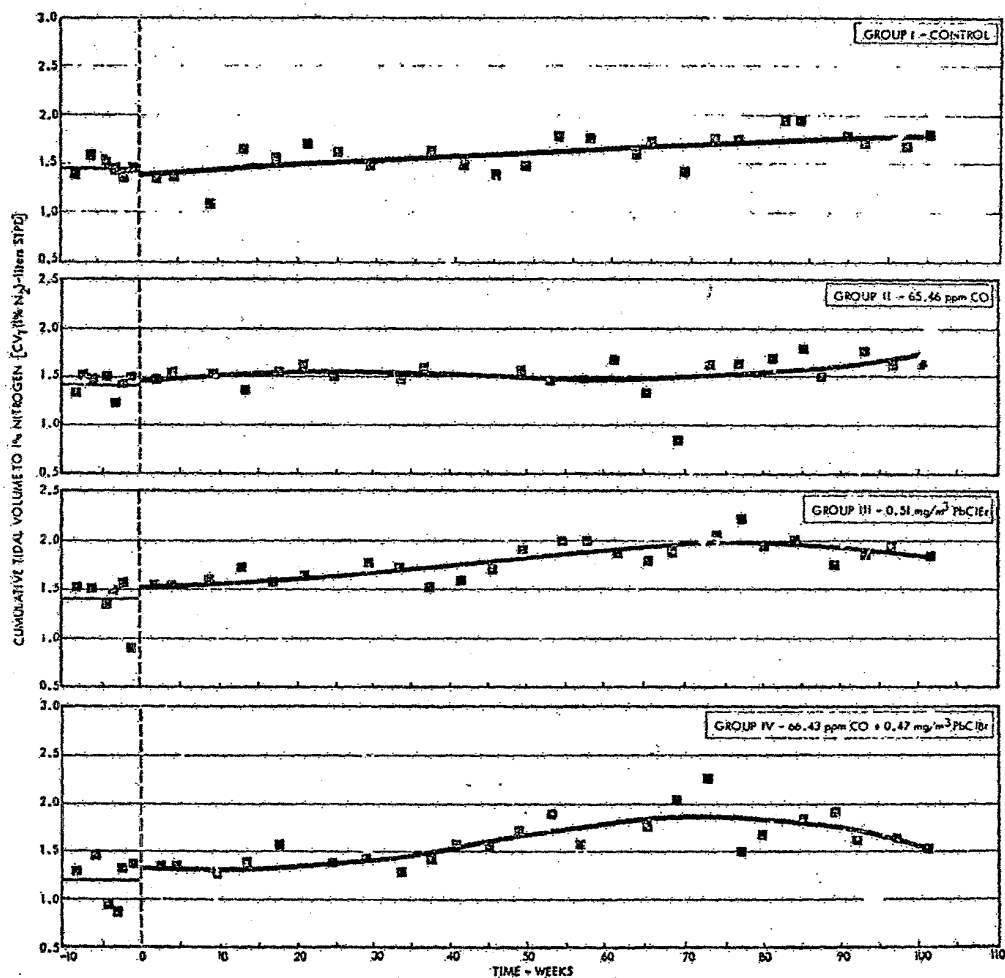


Figure 80 - Third degree polynomial regression curves for CV_T(1% N₂) prior to and during exposure to carbon monoxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.

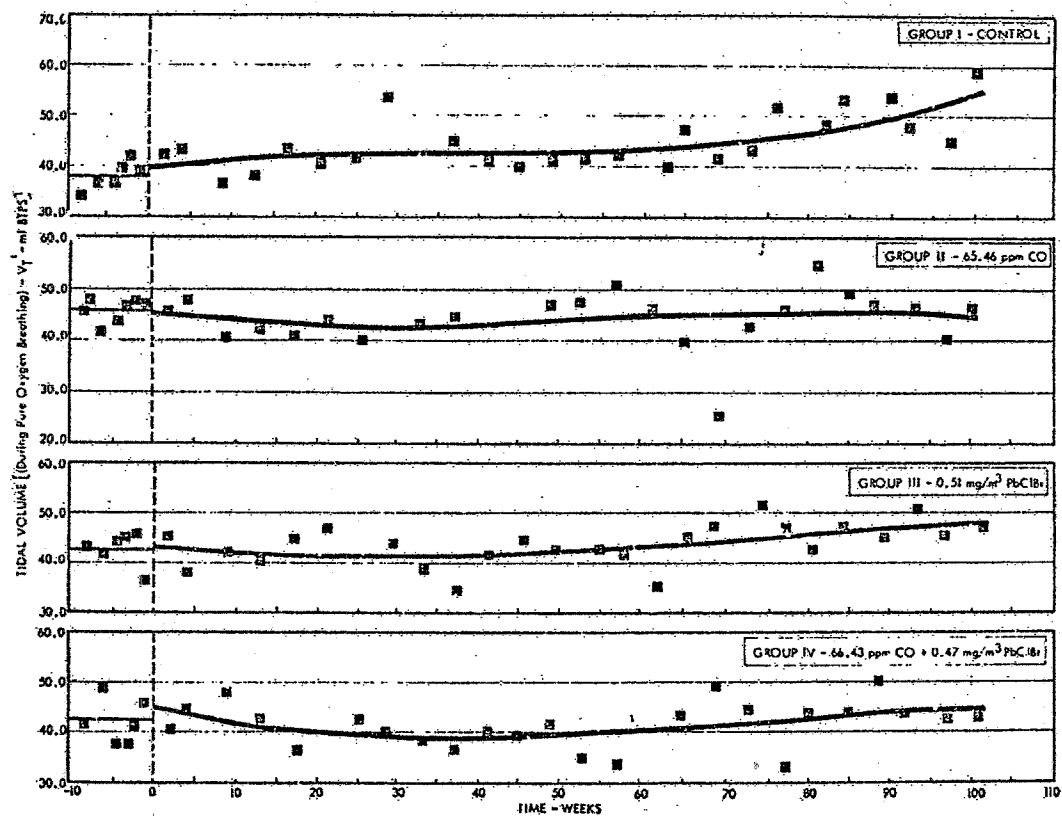


Figure 81 - Third degree polynomial regression curves for V_T' prior to and during exposure to carbon monoxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.



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3.5. Clinical Biochemistry

The group means, standard errors, and the results of the analysis of variance of the various clinical biochemical variables measured are presented in Tables 22 through 35, Appendix D. Scattered statistically significant differences were noted; however, no trends were seen in any of the variables. Throughout the study, the group mean values fluctuated within the normal ranges of these variables.

3.6. Arterial Blood Gas and pH

The group means and standard errors for the blood gas variables are presented in Table 36, Appendix D. Examination of these data did not reveal any consistent trend with time. No apparent exposure-related changes were seen in any of these variables.

3.7. Terminal Body Weight, Organ Weight, and Organ Weight as a Percentage of Body Weight

The data of the terminal body weight, organ weight, and organ/body weight ratios are presented in Tables 37 and 38, Appendix D, for males and females, respectively. Single classification analysis of variance revealed that the brain weight for the males in Group IV was significantly higher than for Group I males. The mean terminal body weight for the females in Group II was higher than the terminal body weight for Group III females. The kidney weight to body weight ratio was higher in Group III females than in Group II females and the heart weight for Group II females was significantly higher than Group I females.



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3.8. Histopathology Summary

A detailed listing of the microscopic alterations seen in the lungs, tracheas, livers, kidneys, peribronchial lymph nodes, and hearts from the animals in the control and exposure groups are found in Table 39, Appendix D. Exposure-related microscopic alterations were seen in the kidneys of the animals exposed to 0.6 mg/m^3 of PbCl_2 . These microscopic alterations were characterized by varying degrees of degeneration of the proximal convoluted tubules. The epithelial cells of the proximal convoluted tubules were slightly vacuolated in some animals and a slight to moderate degree of nuclear vesiculation was present in some animals. Acid fast intranuclear inclusion bodies were seen in seven of the nine animals exposed to 0.6 mg/m^3 of PbCl_2 alone and in five of the nine animals exposed to the combination of 67.5 ppm CO and 0.6 mg/m^3 of PbCl_2 .

Incidental lesions not related to the exposure conditions were seen in the lungs, peribronchial lymph nodes, tracheas, hearts, and livers from the animals in both the control and exposed groups.

Animal No. 157L in the group exposed to 67.5 ppm CO died during the 42nd week of exposure. Microscopic examination of the tissues from this animal revealed lesions consistent with a diagnosis of monkey pox. Necrosis and hemorrhage were seen in the lungs and liver from this animal. Numerous inclusion bodies were present in the epithelial cells of the trachea.



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3.9. Summary

The inhalation exposure of male and female cynomolgus monkeys to 65.46 ppm CO, 0.51 mg/m³ PbClBr, and the combination of 66.43 ppm CO plus 0.47 mg/m³ PbClBr resulted in a deterioration in the distribution of ventilation in the animals in the two groups containing PbClBr. The number of breaths to 1% nitrogen measured during pure oxygen breathing was significantly elevated in the animals in both groups exposed to PbClBr. Cumulative tidal volume to 1% nitrogen and respiratory rate measured during pure oxygen breathing were significantly elevated in the group exposed to 0.51 mg/m³ PbClBr. These latter differences were not seen in the group exposed to the combination of 66.43 ppm CO plus 0.47 mg/m³ PbClBr.

Statistical analyses comparing the control group to the group exposed to 65.46 ppm CO indicated a significant mean difference in the number of breaths to 1% nitrogen, respiratory rate, and tidal volume measured during pure oxygen breathing. However, these differences were attributed to alteration of the sex ratio and hence the animal size distribution due to the deaths (not compound-related) of two male members of the group exposed to 65.46 ppm CO.

Microscopic alterations related to the exposure to PbClBr were found in the kidneys of the animals of these two lead groups. These histopathological changes were characterized by varying degrees of degeneration of the proximal convoluted tubules. The epithelial cells of these tubules were vacuolated and possessed vesiculated nuclei. Numerous intranuclear acid fast inclusion bodies were seen in these epithelial cells.



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Hematological, clinical biochemical, and arterial blood gas measurements made pre-exposure and periodically throughout the exposure period on the animals in the control and exposed groups did not reveal any meaningful differences. No trends were noted in any of these variables, and, in general, the exposed animals were comparable to the controls. Statistical analysis of the body weights measured periodically throughout the exposure period revealed that all animals in both the control and exposed groups increased in weight with time, although the group exposed to 65.46 ppm CO showed a slower mean growth rate which can be attributed to the deaths of two of its male members. No meaningful differences from the controls in terminal body weights, organ weights, and organ/body weight ratios were found for the exposed animals.



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Appendix D - Data compilations and summary of statistical analysis for
Statistical Grouping D, comprised of the following:

Group I - Control, Group II - 65.46 ppm CO, Group III -
0.51 mg/m³ PbClBr, and Group IV - 66.43 ppm CO + 0.47 mg/m³
PbClBr.

Table 1 - Monthly means and the grand mean for the analytical concentrations of carbon monoxide in Group II.

Date	n	$\bar{x}$ ppm	S.D.
4/ 7/68 - 4/31/68	24	52.7229	18.6179
5/ 1/68 - 5/31/68	31	64.9476	3.5378
6/ 1/68 - 6/30/68	30	66.0280	3.2531
7/ 1/68 - 7/31/68	31	65.6890	3.3289
8/ 1/68 - 8/31/68	31	65.2639	2.3260
9/ 1/68 - 9/30/68	30	63.8380	5.0975
10/ 1/68 - 10/31/68	31	63.9106	3.2811
11/ 1/68 - 11/30/68	30	65.2470	2.8750
12/ 1/68 - 12/31/68	31	66.2948	4.1978
1/ 1/69 - 1/31/69	31	65.3729	1.8454
2/ 1/69 - 2/28/69	28	66.9978	2.1481
3/ 1/69 - 3/31/69	31	65.9987	2.4073
4/ 1/69 - 4/30/69	20	67.5077	2.3761
5/ 1/69 - 5/31/69	31	68.1716	2.2823
6/ 1/69 - 6/30/69	30	68.4580	1.9130
7/ 1/69 - 7/31/69	31	66.8609	1.2850
8/ 1/69 - 8/31/69	31	67.4068	1.3534
9/ 1/69 - 9/30/69	30	65.5323	1.9411
10/ 1/69 - 10/31/69	31	65.6203	1.4197
11/ 1/69 - 11/30/69	30	67.1577	1.8847
12/ 1/69 - 12/31/69	31	64.7923	3.4599
1/ 1/70 - 1/31/70	31	65.1948	2.1385
2/ 1/70 - 2/28/70	28	66.7646	2.7352
3/ 1/70 - 3/31/70	31	65.8845	1.7923
4/ 1/70 - 4/ 9/70	9	64.8081	5.7551

N = 25

$\bar{x}$ = 65.46

S.D. = 3.33

Table 2 - Monthly means and the grand mean for the analytical concentrations of lead chlorobromide in Group III.

Date	n	$\bar{x}$ mg/m ³	S.D.
5/1/68 - 5/31/68	20	0.8570	1.0552
6/ 1/68 - 6/30/68	30	0.4743	0.6379
7/ 1/68 - 7/31/68	31	0.4565	0.3048
8/ 1/68 - 8/31/68	31	0.6022	0.1088
9/ 1/68 - 9/30/68	30	0.5773	0.1526
10/ 1/68 - 10/31/68	31	0.5074	0.1497
11/ 1/68 - 11/30/68	30	0.4286	0.1944
12/ 1/68 - 12/31/68	31	0.4638	0.1819
1/ 1/69 - 1/31/69	31	0.4752	0.1339
2/ 1/69 - 2/28/69	28	0.6154	0.7173
3/ 1/69 - 3/31/69	31	0.5677	0.1515
4/ 1/69 - 4/30/69	30	0.5147	0.2131
5/ 1/69 - 5/31/69	31	0.7770	0.1710
6/ 1/69 - 6/30/69	30	0.5503	0.1740
7/ 1/69 - 7/31/69	31	0.5597	0.2216
8/ 1/69 - 8/31/69	31	0.5010	0.1545
9/ 1/69 - 9/30/69	30	0.4737	0.2049
10/ 1/69 - 10/31/69	31	0.5352	0.2722
11/ 1/69 - 11/30/69	30	0.4930	0.0363
12/ 1/69 - 12/31/69	31	0.3871	0.1065
1/ 1/70 - 1/31/70	31	0.4052	0.2503
2/ 1/70 - 2/28/70	28	0.5100	0.3669
3/ 1/70 - 3/31/70	31	0.5561	0.2526
4/ 1/70 - 4/30/70	30	0.3070	0.5732
5/ 1/70 - 5/ 5/70	5	0.1080	0.0295

N = 25

$\bar{X}$ = 0.51

S.D. = 0.27

Table 3 - Monthly means and the grand mean for the analytical concentrations of carbon monoxide and lead chloride for Group IV.

Date	n	CO		PbClBr	
		$\bar{x}$ ppm	S.D.	$\bar{x}$ mg/m ³	S.D.
6/ 1/68 - 6/30/68	30	66.0710	2.5214	0.5133	0.2917
7/ 1/68 - 7/31/68	31	66.4219	2.2956	0.4619	0.2142
8/ 1/68 - 8/31/68	31	65.9890	3.0532	0.5868	0.1252
9/ 1/68 - 9/30/68	30	66.5103	3.7002	0.6360	0.2128
10/ 1/68 - 10/31/68	31	64.8868	3.8590	0.4477	0.1979
11/ 1/68 - 11/30/68	30	64.2883	3.2099	0.3627	0.1645
12/ 1/68 - 12/31/68	31	65.0668	2.3897	0.5590	0.2247
1/ 1/69 - 1/31/69	31	66.0261	1.8732	0.3787	0.1247
2/ 1/69 - 2/28/69	28	65.7504	1.7250	0.3350	0.2189
3/ 1/69 - 3/31/69	31	67.8374	2.1281	0.4094	0.1793
4/ 1/69 - 4/30/69	30	67.2590	2.0255	0.6210	0.3262
5/ 1/69 - 5/31/69	31	66.5474	2.1141	0.4374	0.1435
6/ 1/69 - 6/30/69	30	66.3283	1.3444	0.4703	0.1416
7/ 1/69 - 7/31/69	31	66.2529	1.4520	0.5313	0.1443
8/ 1/69 - 8/31/69	31	67.2252	2.1208	0.5042	0.1467
9/ 1/69 - 9/30/69	30	67.5253	2.2677	0.5493	0.1569
10/ 1/69 - 10/31/69	31	66.4932	2.0110	0.5365	0.2504
11/ 1/69 - 11/30/69	30	66.8467	1.4641	0.5010	0.2181
12/ 1/69 - 12/31/69	31	65.9313	2.8099	0.5203	0.1853
1/ 1/70 - 1/31/70	31	67.0703	2.1003	0.5419	0.2456
2/ 1/70 - 2/28/70	28	67.7143	1.9892	0.5368	0.1744
3/ 1/70 - 3/31/70	31	66.5290	1.5245	0.5568	0.3217
4/ 1/70 - 4/30/70	30	66.1123	1.8950	0.3607	0.2049
5/ 1/70 - 5/13/70	13	67.6277	2.7596	0.4669	0.2514

N = 24
 $\bar{X}$ = 66.43
S.D. = 2.28

N = 24
 $\bar{X}$ = 0.47
S.D. = 0.21

Table 4 - Summary of statistical analyses of body weight data for Statistical Grouping D, comprised of the following: Group I - Control, Group II - 65.46 ppm CO, Group III - 0.51 mg/m³ PbClBr, and Group IV - 65.43 ppm CO + 0.47 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION				
SOURCE OF VARIATION	df	SS	MS	F
Non-Parallelism	3	5.058	1.686	1.77
Error Deviation	902	8.583 x 10 ⁻²	9.515 x 10 ⁻¹	-
				p ≤ .05

FIRST DEGREE POLYNOMIAL REGRESSION COEFFICIENTS				
GROUPS	REGRESSION COEFFICIENTS ± S.E.		SY.X	r
	A	B		
I	2.63 ± 0.052	1.54 x 10 ⁻² ± 8.93 x 10 ⁻⁴	0.14	0.96
II	2.90 ± 0.065	9.97 x 10 ⁻³ ± 1.08 x 10 ⁻³	0.17	0.89
III	2.61 ± 0.046	1.53 x 10 ⁻² ± 8.02 x 10 ⁻⁴	0.13	0.97
IV	2.71 ± 0.049	1.29 x 10 ⁻² ± 8.31 x 10 ⁻⁴	0.13	0.95

Table 5 - Summary of statistical analyses of total respiratory system flow resistance during inspiration data for Statistical Grouping D, comprised of the following: Group I - Control, Group II - 65.46 ppm CO, Group III - 0.51 mg/m³ PbClBr, and Group IV - 66.43 ppm CO + 0.47 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	2.843 × 10 ⁻³	9.476 × 10 ⁻⁴	6.71	Yes
Error Deviation	1115	1.573 × 10 ⁻¹	1.411 × 10 ⁻⁴	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.					SV, x	n	r
	A	B	C	D				
I	0.044 ± 0.0033	2.12 × 10 ⁻⁴ ± 3.81 × 10 ⁻⁴	-9.72 × 10 ⁻⁶ ± 9.30 × 10 ⁻⁶	8.10 × 10 ⁻⁸ ± 6.10 × 10 ⁻⁸		0.008	39	0.37
II	0.042 ± 0.0038	1.34 × 10 ⁻⁴ ± 4.46 × 10 ⁻⁴	-2.29 × 10 ⁻⁷ ± 1.06 × 10 ⁻⁵	-7.00 × 10 ⁻⁹ ± 6.80 × 10 ⁻⁸		0.009	37	0.25
III	0.053 ± 0.0026	-5.52 × 10 ⁻⁴ ± 3.01 × 10 ⁻⁴	5.42 × 10 ⁻⁶ ± 7.35 × 10 ⁻⁶	-2.09 × 10 ⁻⁹ ± 4.30 × 10 ⁻⁸		0.006	39	0.65
IV	0.057 ± 0.0036	-6.36 × 10 ⁻⁴ ± 4.22 × 10 ⁻⁴	1.28 × 10 ⁻⁵ ± 1.07 × 10 ⁻⁵	-7.60 × 10 ⁻⁸ ± 7.30 × 10 ⁻⁸		0.008	37	0.39

Table 20 - Mean values $\pm$ (S.E.) and summary of single classification analysis of variance for blood glucose (Glu. - mg percent) for male and female monkeys in Statistical Grouping A.

Groups	Time-Weeks					
	Pre-exposure -8	4	16	40	68	104
I - Control	57.3 (3.3)	59.6 (3.3)	69.0 (4.4)	94.6 (4.4)	97.3 (5.3)	82.4 (7.6)
II - 0.51 mg/m ³ PbClBr	68.3 (2.9)	51.9 (3.0)	79.9 (2.3)	69.3 (4.3)	93.4 (3.5)	87.3 (5.2)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Groups	Time-Weeks					
	Pre-exposure -8	4	16	40	68	104
I vs II	N.S.	N.S.	SIG	SIG	N.S.	N.S.

Table 21 - Mean values $\pm$ (S.E.) and summary of single classification analysis of variance for blood urea nitrogen (BUN - mg percent) for male and female monkeys in Statistical Grouping A.

Groups	Pre-exposure -8	Time-Weeks				
		4*	16	40	68*	104
I - Control	16.3 (1.0)	19.2 (1.4)	17.0 (0.6)	18.6 (0.5)	22.6 (0.7)	23.2 (1.1)
II - 0.51 mg/m ³ PbClBr	14.4 (0.6)	15.8 (0.5)	8.8 (0.9)	17.7 (0.7)	22.6 (1.6)	19.8 (1.1)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Groups	Time-Weeks					
	Pre-exposure -8	4	16	40	68	104
I vs II	N.S.	SIG	SIG	N.S.	N.S.	N.S.

* The variances of these groups were heterogeneous.

Table 22 - Mean values $\pm$ (S.E.) and summary of single classification analysis of variance for total serum bilirubin (mg percent) for male and female monkeys in Statistical Grouping A.

Groups	Time-Weeks				
	Pre-exposure -8	4	16	40	68
I - Control	0.27 (0.04)	0.26 (0.03)	0.26 (0.02)	0.30 (0.03)	0.29 (0.03)
II - 0.51 mg/m ³ PbClBr	0.17 (0.02)	0.27 (0.02)	0.28 (0.03)	0.40 (0.02)	0.26 (0.02)
					0.49 (0.07)
					0.33 (0.02)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Groups	Time-Weeks				
	Pre-exposure -8	4	16	40	68
I vs II	SIG	N.S.	N.S.	SIG	N.S.
					SIG

* The variances of these groups were heterogeneous.

Table 23 - Mean values $\pm$ (S.E.) and summary of single classification analysis of variance for total serum protein (grams percent) for male and female monkeys in Statistical Grouping A.

Groups	Time-Weeks					
	Pre-exposure -8	4	16 *	40	68	104
I - Control	7.30 (0.14)	7.76 (0.13)	8.24 (0.11)	7.88 (0.21)	7.44 (0.13)	7.56 (0.10)
II - 0.51 mg/m ³ PbClBr	7.53 (0.17)	7.74 (0.19)	7.75 (0.22)	7.19 (0.12)	7.00 (0.13)	7.28 (0.16)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Groups	Time-Weeks					
	Pre-exposure -8	4	16	40	58	104
I vs II	N.S.	N.S.	N.S.	SIG	SIG	N.S.

* The variances of these groups were heterogeneous.

Table 24 - Mean values $\pm$ (S.E.) and summary of single classification analysis of variance for serum albumin (grams percent) for male and female monkeys in Statistical Grouping A.

Groups	Time-Weeks					
	Pre-exposure -8 *	4	16	40	68 *	104
I - Control	2.56 (0.15)	2.58 (0.05)	3.10 (0.07)	2.87 (0.08)	2.45 (0.12)	2.74 (0.07)
II - 0.5) mg/m ³ PbClBr	2.40 (0.05)	2.80 (0.05)	2.48 (0.05)	2.36 (0.06)	2.56 (0.06)	2.59 (0.07)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Groups	Time-Weeks					
	Pre-exposure -8	4	16	40	68	104
I vs II	N.S.	SIG	SIG	SIG	N.S.	N.S.

* The variances of these groups were heterogeneous.

Table 26 - Mean values $\pm$ (S.E.) and summary of single classification analysis of variance for serum potassium (K-meq/liter) for male and female monkeys in Statistical Grouping A.

Groups	Time-Weeks					
	Pre-exposure -8 *	4	16	40	68	104*
I - Control	3.75 (0.24)	3.67 (0.20)	3.64 (0.22)	3.81 (0.13)	4.02 (0.11)	3.56 (0.10)
II - 0.51 mg/m ³ PbClBr	3.62 (0.10)	3.77 (0.24)	3.85 (0.19)	3.89 (0.11)	3.86 (0.15)	3.81 (0.24)

Comparison of Experimental Treatment Effects ($p < .05$)

Groups	Time-Weeks					
	Pre-exposure -8	4	16	40	68	104
I vs II	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.

* The variances of these groups were heterogeneous.

Table 25 - Mean values $\pm$ (S.E.) and summary of single classification analysis of variance for serum sodium (Na - meq/liter) for male and female monkeys in Statistical Grouping A.

Groups	Time-Weeks					
	Pre-exposure -8	4	16	40	68	104
I - Control	148.0 (0.5)	143.7 (0.3)	139.2 (0.7)	148.7 (0.6)	145.7 (0.8)	148.7 (0.7)
II - 0.51 mg/m ³ PBClBr	147.1 (0.5)	145.0 (0.7)	141.7 (0.5)	143.0 (0.3)	147.9 (0.8)	148.4 (0.6)
Comparison of Experimental Treatment Effects ($p \leq .05$)						
Groups	Time-Weeks					
	Pre-exposure -8	4	16	40	68	104
I vs II	N.S.	N.S.	SIG	SIG	N.S.	N.S.

Table 25 - Mean values $\pm$ (S.E.) and summary of single classification analysis of variance for serum sodium (Na - mEq/liter) for male and female monkeys in Statistical Grouping A.

Groups	Time-Weeks					
	Pre-exposure -8	4	16	40	68	104
I - Control	148.0 (0.5)	143.7 (0.3)	139.2 (0.7)	148.7 (0.6)	145.7 (0.8)	148.7 (0.7)
II - 0.51 mg/m ² PbCl ₂	147.1 (0.5)	145.0 (0.7)	141.7 (0.5)	143.0 (0.3)	147.9 (0.8)	148.4 (0.6)
Comparison of Experimental Treatment Effects ($p < .05$)						
Groups	Time-Weeks					
	Pre-exposure -8	4	16	40	68	104
I vs II	N.S.	N.S.	SIG	SIG	N.S.	N.S.

Table 26 - Mean values $\pm$ (S.E.) and summary of single classification analysis of variance for serum potassium (K-meq/liter) for male and female monkeys in Statistical Grouping A.

Groups	Time-Weeks					
	Pre-exposure -8 *	4	16	40	68	104*
I - Control	3.75 (0.24)	3.67 (0.20)	3.64 (0.22)	3.81 (0.13)	4.02 (0.11)	3.56 (0.10)
II - 0.51 mg/m ³ PbClBr	3.62 (0.10)	3.77 (0.24)	3.85 (0.19)	3.89 (0.11)	3.86 (0.15)	3.81 (0.24)
Comparison of Experimental Treatment Effects ($p \leq .05$)						
Groups	Time-Weeks					
	Pre-exposure -8	4	16	40	68	104
I vs II	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.

* The variances of these groups were heterogeneous.

Table 27 - Mean values $\pm$ (S.E.) and summary of single classification analysis of variance for serum chlorides (Cl - mcg/titer) for male and female monkeys in Statistical Grouping A.

Groups	Time-Weeks					
	Pre-exposure -8 *	4	16	40	68	104*
I - Control	111.9 (1.2)	109.6 (0.6)	108.3 (1.1)	107.7 (0.9)	110.1 (0.8)	112.7 (1.4)
II - 0.51 mg/m ³ PbClBr	112.9 (0.5)	103.2 (0.4)	109.9 (0.6)	114.6 (0.4)	111.4 (0.8)	112.2 (0.4)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Groups	Time-Weeks					
	Pre-exposure -8	4	16	40	68	104
I vs II	N.S.	SIG	N.S.	SIG	N.S.	N.S.

* The variances of these groups were heterogeneous.

Table 28 - Mean values $\pm$ (S.E.) and summary of single classification analysis of variance for serum carbon dioxide (CO_2 - mEq/liter) for male and female monkeys in Statistical Grouping A.

Groups	Time-Weeks					
	Pre-exposure -8	4	16*	40	68	104*
I - Control	24.8 (1.0)	24.3 (0.8)	28.9 (0.7)	27.6 (0.5)	26.4 (0.7)	25.8 (0.6)
II - 0.51 mg/m ³ PbClBr	26.7 (0.6)	25.7 (0.9)	22.9 (1.7)	29.4 (1.0)	26.5 (0.5)	24.6 (1.4)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Groups	Time-Weeks					
	Pre-exposure -8	4	16	40	68	104
I vs II	N.S.	N.S.	SIG	N.S.	N.S.	N.S.

*The variances of these groups were heterogeneous.

Table 29 - Mean values $\pm$ (S.E.) and summary of single classification analysis of variance for serum calcium (Ca - mg percent) for male and female monkeys in Statistical Grouping A.

Groups	Time-Weeks				
	Pre-exposure -8	4	16 *	40	68 [*] 104
I - Control	9.47 (0.23)	9.36 (0.12)	10.16 (0.08)	11.13 (0.10)	9.54 (0.30) 9.88 (0.13)
II - 0.51 mg/m ³ PbClBr	9.77 (0.13)	9.32 (0.11)	9.34 (0.23)	10.03 (0.15)	9.90 (0.13) 10.01 (0.16)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Groups	Time-Weeks				
	Pre-exposure -8	4	16	40	68 104
I vs II	N.S.	N.S.	SIG	SIG	N.S. N.S.

* The variances of these groups were heterogeneous.

Table 30 - Mean values $\pm$ (S.E.) and summary of single classification analysis of variance for serum glutamic oxaloacetic transaminase (SGOT - K units) for male and female monkeys in Statistical Grouping A.

Groups	Time-Weeks				
	Pre-exposure -8 *	4	16*	40*	68 * 104
I - Control	26.0 (4.9)	45.3 (3.2)	20.2 (0.8)	33.6 (3.6)	97.2 (21.4) 47.0 (6.2)
II - 0.51 mg/m ³ PbClBr	30.1 (2.1)	31.6 (2.2)	57.0 (10.7)	47.1 (7.8)	52.4 (4.0) 44.6 (5.4)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Groups	Time-Weeks				
	Pre-exposure -8	4	16	40	68 104
I vs II	N.S.	SIG	SIG	N.S.	N.S.

* The variances of these groups were heterogeneous.

Table 31 - Mean values $\pm$ (S.E.) and summary of single classification analysis of variance for serum glutamic pyruvic transaminase (SGPT - RF units) for male and female monkeys in Statistical Grouping A.

Groups	Time-Weeks				
	Pre-exposure -8	4	16	40 *	68 * 104*
I - Control	15.4 (2.8)	20.7 (3.1)	25.1 (2.7)	41.2 (8.6)	41.3 (2.9) 40.7 (3.7)
II - 0.51 mg/m ³ PbClBr	26.3 (2.5)	27.7 (1.5)	20.2 (3.1)	29.5 (5.0)	47.4 (0.7) 42.6 (8.1)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Groups	Time-Weeks				
	Pre-exposure -8	4	16	40	68 104
I vs II	SIG	N.S.	N.S.	N.S.	SIG N.S.

* The variances of these groups were heterogeneous.

Table 32 - Mean values $\pm$ (S.E.) and summary of single classification analysis of variance for lactic acid dehydrogenase (LDH - WROB units) for male and female monkeys in Statistical Grouping A.

Groups	Time-Weeks					
	Pre-exposure -8	4	16 *	40 *	68	104 *
I - Control	512 (99)	746 (49)	572 (80)	832 (221)	1573 (156)	597 (93)
II - 0.51 mg/m ³ PbClBr	926 (56)	793 (82)	821 (173)	662 (69)	1306 (129)	440 (42)

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Comparison of Experimental Treatment Effects ($p \leq .05$)

Groups	Time-Weeks					
	Pre-exposure -8	4	16	40	68	104
I vs II	SIG	N.S.	N.S.	N.S.	N.S.	N.S.

* The variances of these groups were heterogeneous.

Table 33 - Mean values $\pm$ (S.E.) and summary of single classification analysis of variance for alkaline phosphatase (Alk. P04 - KA units) for male and female monkeys in Statistical Grouping A.

Groups	Time-Weeks					
	Pre-exposure -8	4	16	40*	68	104
I - Control	57.2 (11.3)	58.6 (12.9)	55.2 (8.3)	48.4 (5.4)	41.9 (7.3)	48.4 (8.7)
II - 0.51 mg/m ³ PbClBr	54.4 (8.6)	50.7 (6.9)	67.5 (9.9)	56.3 (10.8)	49.1 (8.4)	41.4 (7.6)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Groups	Time-Weeks					
	Pre-exposure -8	4	16	40	68	104
I vs II	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.

* The variances of these groups were heterogeneous.

Table 34 - Mean values $\pm$ (S.E.) for blood gas and pH variables measured in male and female monkeys in Statistical Grouping A, comprised of the following: Group I - Control and Group II - 0.51 mg/m³ PbCl₂.

Interval Week	PO ₂		PCO ₂		pH	
	Group I	Group II	Group I	Group II	Group I	Group II
-3	91.6 (2.0)	87.4 (1.7)	39.9 (0.7)	41.0 (0.8)	7.38 (0.00)	-
1	87.8 (1.8)	91.9 (2.7)	37.2 (1.0)	43.8 (1.2)	7.37 (0.00)	7.35 (0.01)
6	87.8 (1.9)	88.9 (1.9)	44.4 (1.0)	37.9 (1.1)	-	7.37 (0.00)
13	87.5 (0.9)	90.5 (1.3)	39.8 (1.3)	38.2 (1.1)	7.37 (0.00)	7.37 (0.01)
26	89.6 (1.9)	84.5 (1.1)	40.3 (1.2)	38.7 (0.6)	7.38 (0.01)	7.37 (0.01)
39	85.8 (1.2)	88.4 (1.1)	40.4 (1.8)	37.4 (1.3)	7.38 (0.00)	7.35 (0.01)
65	86.5 (1.6)	86.5 (1.7)	46.1 (1.6)	47.4 (0.8)	7.38 (0.00)	7.36 (0.00)
78	91.6 (1.6)	97.7 (2.8)	42.2 (1.4)	51.9 (1.1)	7.35 (0.01)	7.34 (0.01)
91	98.5 (2.6)	94.5 (2.4)	51.1 (2.4)	49.8 (1.5)	7.37 (0.01)	7.39 (0.01)
104	96.4 (2.2)	83.7 (1.0)	39.8 (1.5)	39.1 (0.9)	7.36 (0.01)	7.34 (0.00)

Table 35 - Mean values $\pm$ (S.D.) and summary of single classification analysis of variance for terminal body weight (g.), organ weight (g.), and organ/body weight ratios (%) for male monkeys for Statistical Grouping A, comprised of the following: Group I - Control and Group II - 0.51 mg/m³ PbC:Br.

Groups	Terminal Body Weight	Brain		Thyroid		Lung		Heart		Liver		Kidneys		Adrenals	
		wt.	ratio	wt.	ratio	wt.	ratio	wt.	ratio*	wt.	ratio	wt.	ratio	wt.	ratio
I	4920 (1410)	73.8 (7.7)	1.57 (0.31)	0.53 (0.34)	0.010 (0.004)	27.8 (6.0)	0.58 (0.08)	16.6 (4.6)	0.34 (0.05)	88.1 (13.3)	1.85 (0.25)	18.6 (4.6)	0.38 (0.05)	0.63 (0.13)	0.013 (0.002)
II	4720 (2252)	67.3 (3.5)	1.59 (0.45)	0.41 (0.13)	0.009 (0.003)	28.2 (9.9)	0.62 (0.07)	16.4 (7.4)	0.35 (0.01)	84.8 (26.6)	1.88 (0.27)	18.3 (7.6)	0.39 (0.05)	0.76 (0.35)	0.016 (0.003)
Significant Differences ($p \leq .05$)															
I vs II	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.

* The variance of this group was heterogeneous.

Table 36 - Mean values $\pm$ (S.D.) and summary of single classification analysis of variance for terminal body weight (g.), organ weight (g.), and organ/body weight ratios (%) for female monkeys for Statistical Grouping A, comprised of the following: Group I - Control and Group II - 0.51 mg/m³ PbCl₂Br.

Groups	Terminal Body Weight	Brain		Thyroid		Lung		Heart		Liver		Kidneys		Adrenals	
		wt.	ratio	wt.	ratio	wt.	ratio	wt.	ratio*	wt.	ratio	wt.	ratio	wt.	ratio*
I	3075 (206)	59.5 (3.1)	1.94 (0.13)	0.43 (0.09)	0.014 (0.004)	21.6 (2.4)	0.70 (0.08)	9.7 (0.8)	0.31 (0.01)	66.3 (4.4)	2.16 (0.17)	13.2 (1.4)	0.43 (0.04)	0.75 (0.29)	0.025 (0.010)
II	2750 (342)	58.9 (6.3)	2.16 (0.32)	0.30 (0.11)	0.011 (0.004)	20.7 (2.8)	0.75 (0.05)	10.2 (2.7)	0.37 (0.05)	59.0 (9.7)	2.14 (0.14)	13.7 (1.8)	0.50 (0.05)	0.69 (0.13)	0.025 (0.002)

Significant Differences ($p \leq .05$)

I vs II N.S. N.S. N.S. N.S. N.S. N.S. N.S. N.S. N.S. N.S. N.S. N.S. N.S. N.S. N.S.

* The variances of these groups were heterogeneous.

Table 37 - Histopathology incidence table for Statistical Grouping A, comprised of the following: Group I - Control and Group II - 0.51 mg/m³ PbClBr.

GROUPS			
I	II		
2/9	2/9	Focal Pleural Thickening	
1/9	3/9	Peribronchial Brown Pigment	
4/9	0/9	Artifactual Emphysema	
9/9	2/9	Alveolar Duct Fibrosis	
0/9	1/9	Thickening Bronchiolar Wall	
0/9	0/9	Bronchiolar Epithelial Hyperplasia	
0/9	0/9	Bronchiolar Epithelial Hypertrophy	
1/9	1/9	Pneumocyte Hyperplasia	
1/9	0/9	Peribronchial Lymphoid Hyperplasia	
0/9	0/9	Emphysema	
0/9	0/9	Focal Necrosis	
0/9	0/9	Focal Hemorrhage	
0/9	0/9	Parasite	
0/9	0/9	Perivascular Edema	
0/9	0/9	Pulmonary Edema	
0/9	1/9	Bronchiolitis	
0/9	0/9	Monkey Pox	
1/9	0/9	Vasculitis	
0/9	0/9	Granuloma	
0/9	0/9	Pneumonitis	
0/9	0/9	Abscess	
1/9	0/9	Lung Mite Infestation	
0/9	0/9	Adenomatosis	
0/9	0/9	Bronchiectasis	
0/9	0/9	Purulent Pneumonia	
0/9	0/9	Epithelial Necrosis	
0/9	0/9	Thickened Alveolar Wall	
0/9	0/9	Pleuritis	
2/9	0/9	Crystalline Material (yellow)	
0/9	0/9	Mucous	
0/9	0/9	Focal Fibrosis	
0/9	0/9	Pleural Fibrosis	
2/9	0/9	Alveolar Wall Fibrosis	
0/9	0/9	Vacuolated Media	
0/9	0/9	Endothelial Hyperplasia	
0/9	0/9	Stenotic	
0/9	0/9	Chronic Pneumonia	
0/9	0/9	Eroded Bronchi	
0/9	0/9	Emphysematous Bulla	

LUNG

Table 37 - Continued

GROUPS			
I	II		
LUNG - Continued			
0/9	0/9	Atelectasis	
0/9	0/9	Congested	
0/9	0/9	Extravasated Blood	
0/9	0/9	Collapsed Alveolar Wall	
LIVER			
0/9	3/9	Pericholangitis	
1/9	3/9	Bile Duct Proliferation	
0/9	0/9	Focal Necrosis	
2/9	0/9	Stenoidal Pigment	
0/9	2/9	Focal Hepatitis	
1/9	0/9	Focal Lymphoid Infiltration	
0/9	0/9	Nematodiasis	
0/9	0/9	Thick Capsule	
0/9	0/9	Granuloma	
0/9	0/9	Abscess	
0/9	0/9	Hepatocyte Vacuolation	
0/9	1/9	Greenish Granular Material in	
0/9	0/9	the Hepatocytes	
PERIBRONCHIAL LYMPH NODE			
6/9	6/9	Phagocytized Pigment	
8/9	0/9	Lymphoid Activity	
0/9	0/9	Lymphoid Atrophy	
0/9	0/9	Adenitis	
1/9	0/9	Granuloma	
1/9	0/9	Reticuloendothelial Cell Hyperplasia	
0/9	0/9	Lymphadenitis	
TRACHEA			
1/9	0/9	Tracheitis	
0/9	0/9	Increase in Goblet Cells	
0/9	0/9	Exudate in Lumen	
0/9	0/9	Necrosis of the Epithelium	
0/9	0/9	Inclusion Bodies	
0/9	0/9	Epithelial Hyperplasia	
0/9	0/9	Cilia Atrophy	
0/9	0/9	Squamous Metaplasia	
0/9	0/9	Focal Hemorrhage	



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A single classification analysis of variance was used for those statistical groupings which did not constitute a factorial design. This analysis includes a test for homogeneity of variances by the method of Bartlett (36). If homogeneous variances were found, the analysis of variances was then performed. When a significant F value was obtained, significance of group differences was determined by Scheffe's method of multiple group comparisons (37). In those instances of heterogeneous variances, a log transform (38) was performed on the data and the test for homogeneity was performed again. If the transformed data had homogeneous variances, the analyses described above were performed. If heterogeneous variances still existed, comparison of individual groups was made by a t-test for unequal variances (38). This single classification analysis of variance without log transform was also used for the organ weight and organ weight/body weight ratio data, terminal body weights, and osmotic fragility of erythrocytes.

6.2.5. Significance Level

All statistical analyses used .05 as the significant probability level, with two-tailed t-tests and one-tailed F-test.



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7. APPENDICES

Following each statistical grouping's summary of results (Section 2.9) will be found an appendix containing a statistical table for each measured parameter, including chamber concentrations. The tables which contain the analysis of variance of linear regression for non-parallelism also include the third degree polynomial regression coefficients corresponding to the fitted curves appearing in the text.



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III. STATISTICAL GROUPING A - RESULTS OF THE CHRONIC EXPOSURE OF CYNOMOLGUS MONKEYS TO 0.51 MG/M³ LEAD CHLOROBROMIDE (PbClBr).

Two groups of animals comprise the first statistical grouping - A. One group was maintained as the control group exposed to filtered room air, a second group was exposed to lead chlorobromide alone. Group designations used throughout this section are presented in Table 10.

Table 10 - Group A designations

<u>Group Designation (No.)</u>	<u>Agent</u>	<u>Nominal Concentration</u>	<u>Mean Analytical Concentration</u>
I (1)	Control	0	0
II (9)	PbClBr	0.60 mg/m ³	0.51 mg/m ³

1. Exposure Concentrations

The chamber concentrations of lead chlorobromide as determined analytically are presented in Table 1, Appendix A, for Group II. The mean standard deviation for this group after 104 weeks of exposure was 0.51 mg/m³ ± 0.27.

2. Particle Size Determination

The mean and geometric deviation of all count particle size determinations for PbClBr converted to mass median diameter (MMD) was 0.55μ ± 1.57 for Group II. A composite size vs. distribution graph constructed on log-probability paper from the pooled count data is presented in Figure 17.

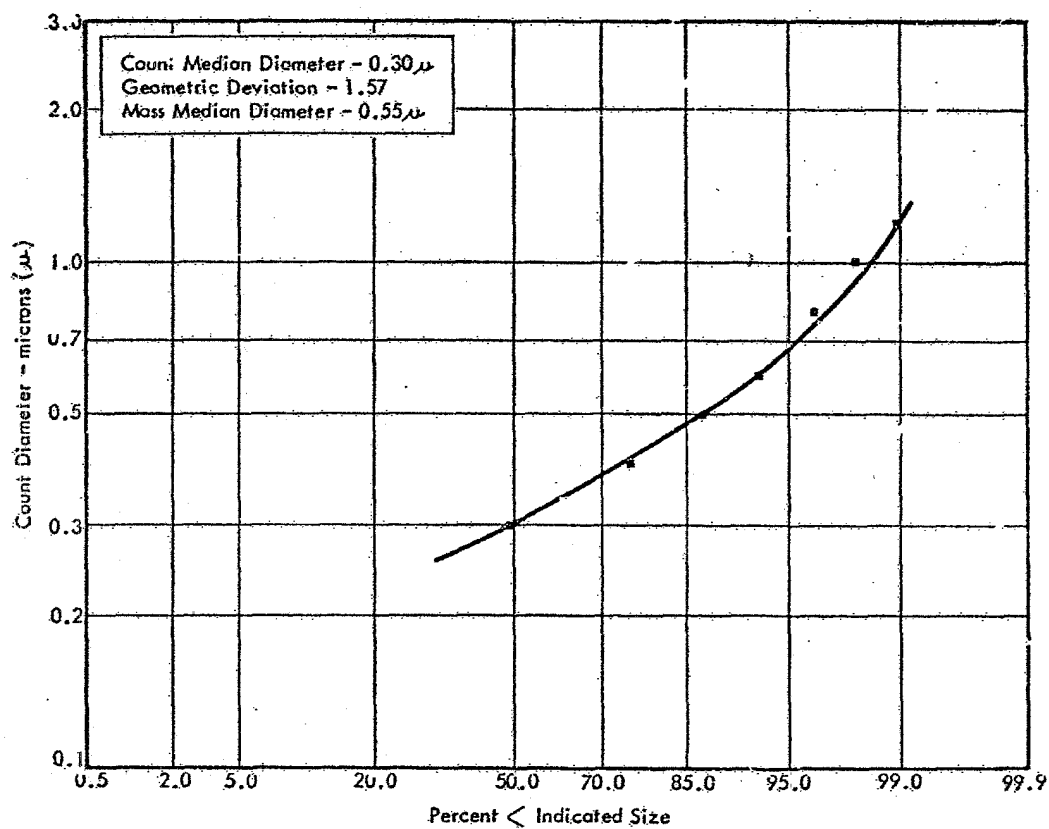


Figure 17 - Particle size distributions (count diameter) of PbClBr.



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3. Biological Measurements

3.1. Body Weight

Analysis of variance of regression for body weight (Table 2, Appendix A) indicated significant slopes among the groups. As expected, the data indicated a trend towards increasing body weight values in both groups and growth rate was similar in all groups. Figure 18 presents the linear regression curves for the two groups.

3.2. Survival

No deaths occurred in Groups I and II during the 104-week exposure period. Daily observation of the animals revealed no clinical signs of toxicity or abnormal behavior during the exposure period.

3.3. Pulmonary Function Tests

3.3.1. Mechanical Properties of the Lung and Respiratory System

3.3.1.1. Total Respiratory System Flow Resistance During Inspiration [Rrs(i)]

Analysis of variance of regression for Rrs(i) (Table 3, Appendix A) revealed no significant slope difference between the groups. The third degree polynomial regression curves are shown in Figure 19. The apparent increase in Group II, relative to Group I, in the first nine weeks was tested for significance by a t-test of the pre-exposure adjusted means of this exposure interval and proved to be significant ($t = 4.33$, d.f. = 16).

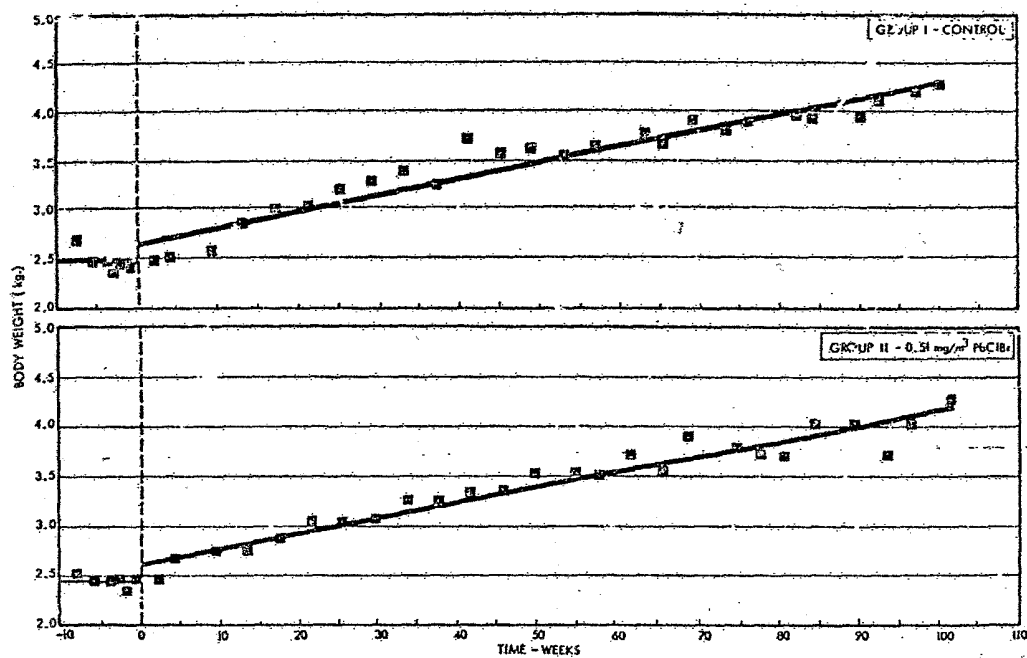


Figure 18 - First degree polynomial regression curves for body weight prior to and during exposure to lead chlorobromide. Each point represents the mean for the animals tested at the indicated time for the various groups.

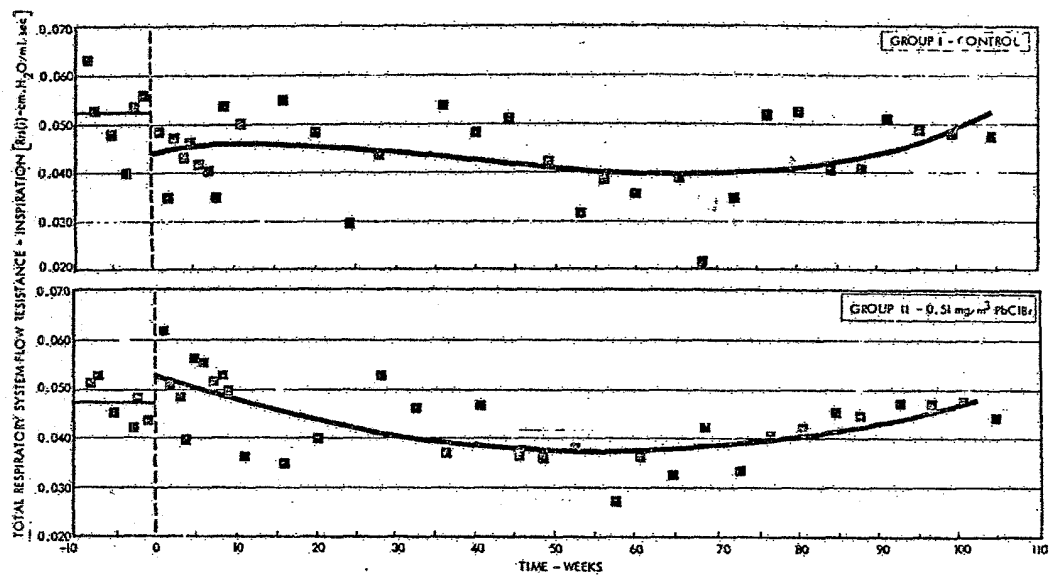


Figure 19 - Third degree polynomial regression curves for Rrs(i) prior to and during exposure to lead chlorobromide. Each point represents the mean for the animals tested at the indicated time for the various groups.



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3.3.1.2. Total Respiratory System Flow Resistance During Expiration [Rrs(e)]

Analysis of variance of regression for Rrs(e) (Table 4, Appendix A) indicated no significant slope difference between the two groups. Figure 20 presents the third degree polynomial regression curves. A t-test of pre-exposure adjusted overall exposure means comparing Groups I and II was not significantly different ($t = 1.92$, d.f. = 16).

3.3.1.3. Tidal Volume (V_T)

Analysis of variance of regression for V_T (Table 5, Appendix A) revealed no significant slope difference between the groups. Figure 21 presents the third degree polynomial regression curves.

3.3.1.4. Respiratory Rate (RR)

Analysis of variance of regression for RR (Table 6, Appendix A) indicated non-parallelism between the groups. The third degree polynomial regression curves (Figure 22) indicated that the non-parallelism was due to the abrupt increase in Group I at the start of the "exposure" period.

3.3.1.5. Dynamic Compliance of the Lung [Cdyn(1)]

Analysis of variance of regression for Cdyn(1) (Table 7, Appendix A) revealed no significant slope difference between the groups. The third degree polynomial regression curves are shown in Figure 23. Although the pre-exposure adjusted means of the first year were significantly different ($t = 2.69$, d.f. = 16), the fact that Group I showed a large increase at the start of exposure renders any interpretation difficult.

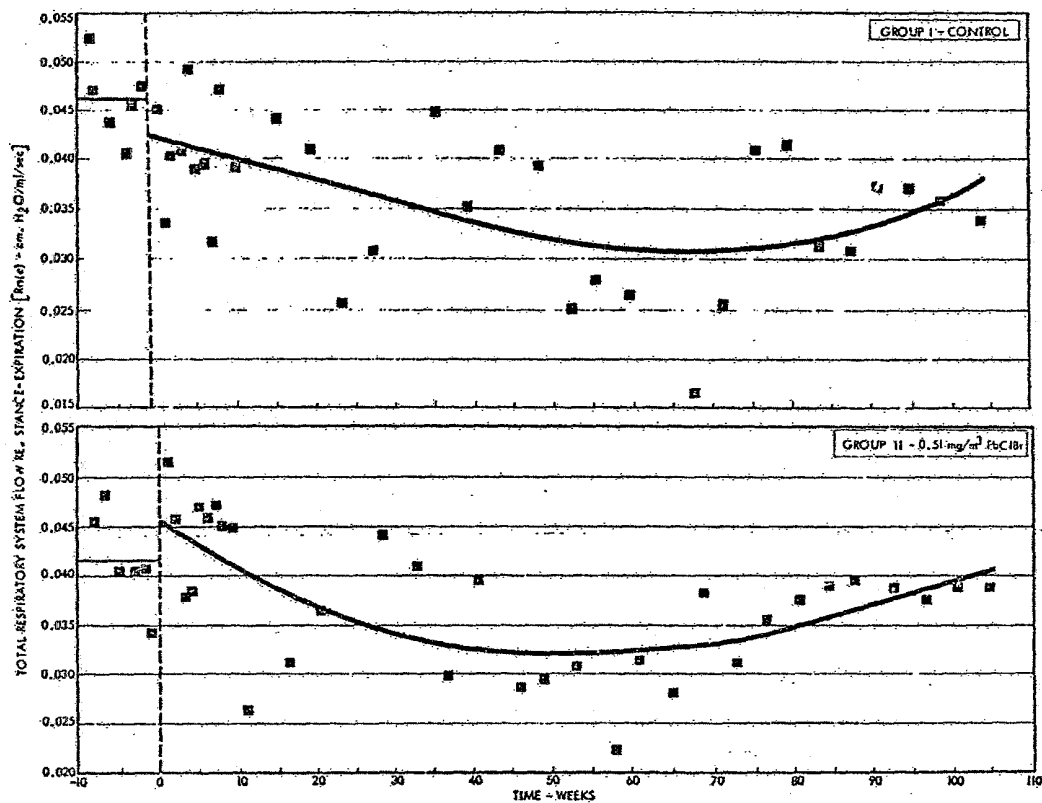


Figure 20 - Third degree polynomial regression curves for $Rrs(e)$ prior to and during exposure to lead chlorobromide. Each point represents the mean for the animals tested at the indicated time for the various groups.

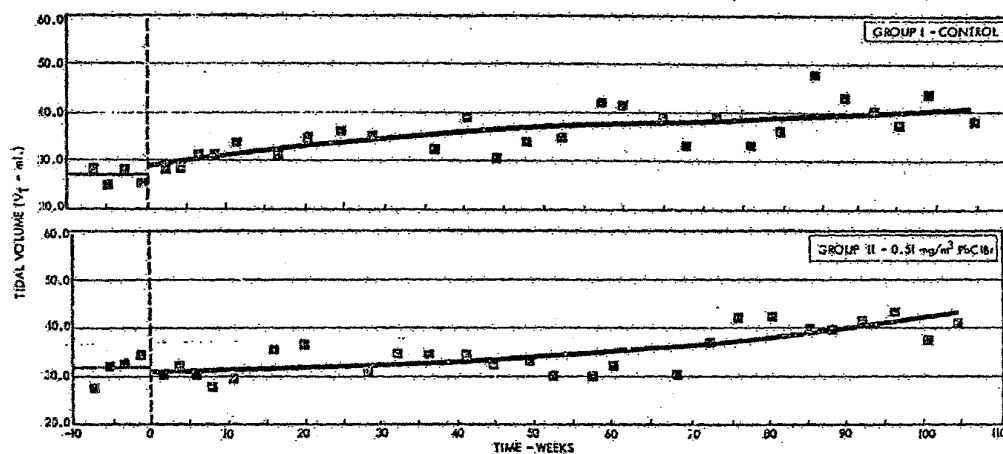


Figure 21 - Third degree polynomial regression curves for V_t prior to and during exposure to lead chlorobromide. Each point represents the mean for the animals tested at the indicated time for the various groups.

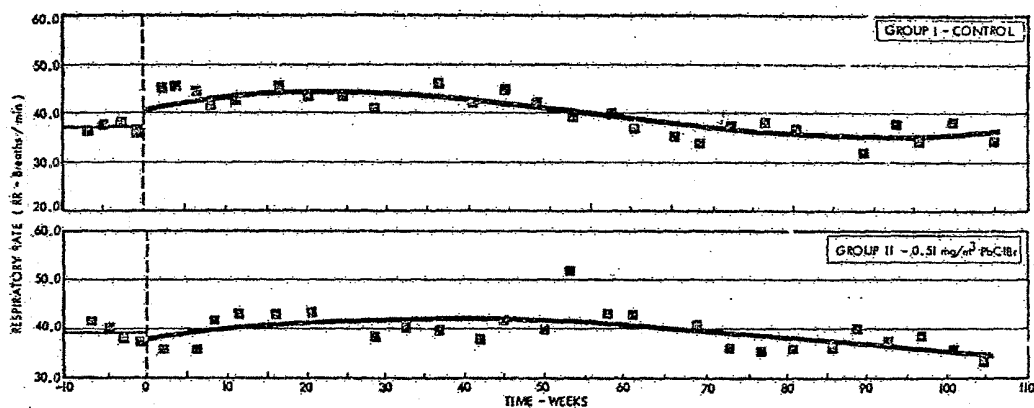


Figure 22 - Third degree polynomial regression curves for RR prior to and during exposure to lead chlorobromide. Each point represents the mean for the animals tested at the indicated time for the various groups.

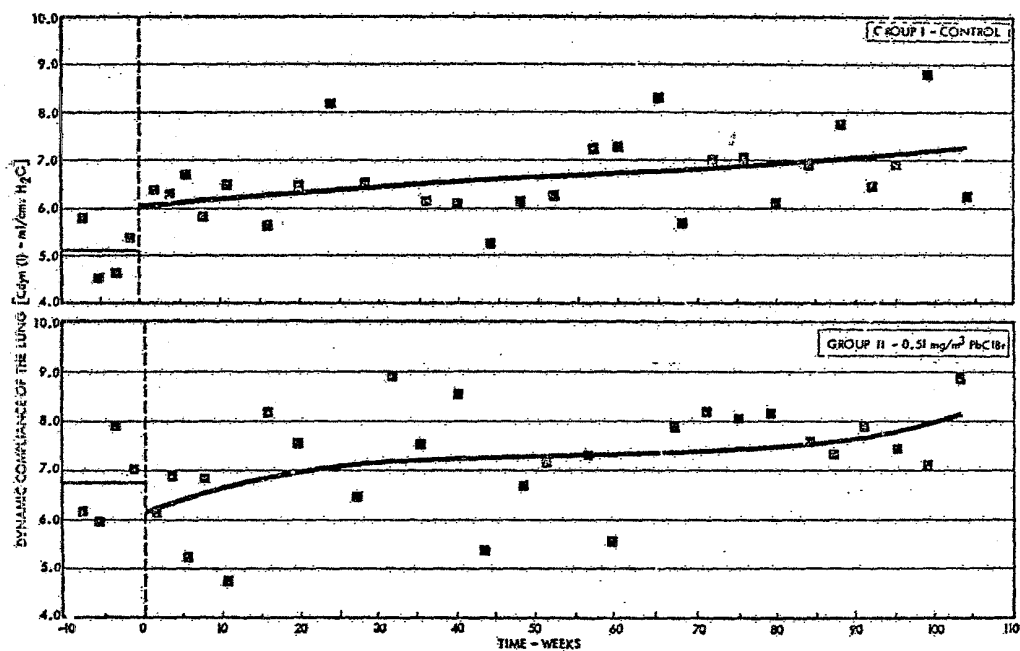


Figure 23 - Third degree polynomial regression curves for $C_{dyn}(1)$ prior to and during exposure to lead chlorobromide. Each point represents the mean for the animals tested at the indicated time for the various groups.



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3.3.1.6. Pulmonary Flow Resistance (R_l)

Analysis of variance of regression for R_l (Table 8, Appendix A) indicated non-parallelism and significant slopes among the groups. The third degree polynomial regression curves (Figure 24) indicated that while there was a difference between the groups at the beginning of exposure (Week 2), there was also an opposite difference at the end of exposure (Week 104). A t-test of the pre-exposure adjusted means of the first nine weeks of exposure showed that Group II was significantly higher than Group I during this period ($t = 2.66$, d.f. = 16).

3.3.1.7. Work of Breathing During Inspiration per ml Tidal Volume [$W(i)/ml V_T$]

Analysis of variance of regression for $W(i)/ml V_T$ (Table 9, Appendix A) revealed no significant slope difference between the groups. The third degree polynomial regression curves, shown in Figure 25, indicated that $W(i)/ml V_T$ values for Group II were lower than Group I throughout the exposure period.

3.3.1.8. Work of Breathing During Expiration per ml Tidal Volume [$W(e)/ml V_T$]

Analysis of variance of regression for $W(e)/ml V_T$ (Table 10, Appendix A) indicated no significant slope difference between the two groups. The third degree polynomial regression curves are presented in Figure 26.

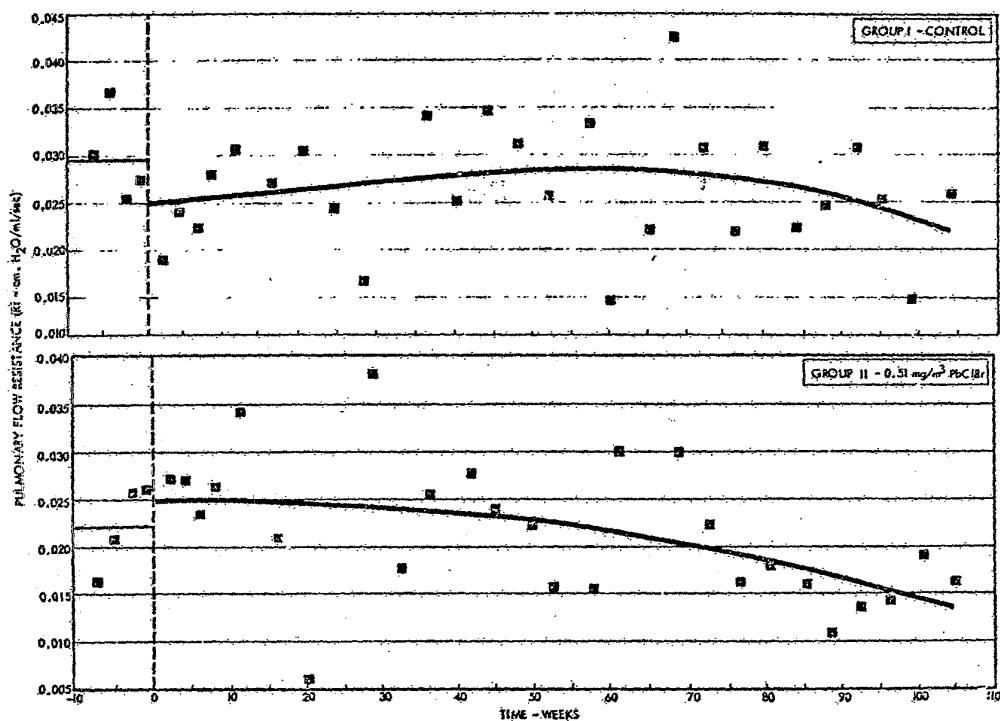


Figure 24 - Third degree polynomial regression curves for Rl prior to and during exposure to lead chlorobromide. Each point represents the mean for the animals tested at the indicated time for the various groups.

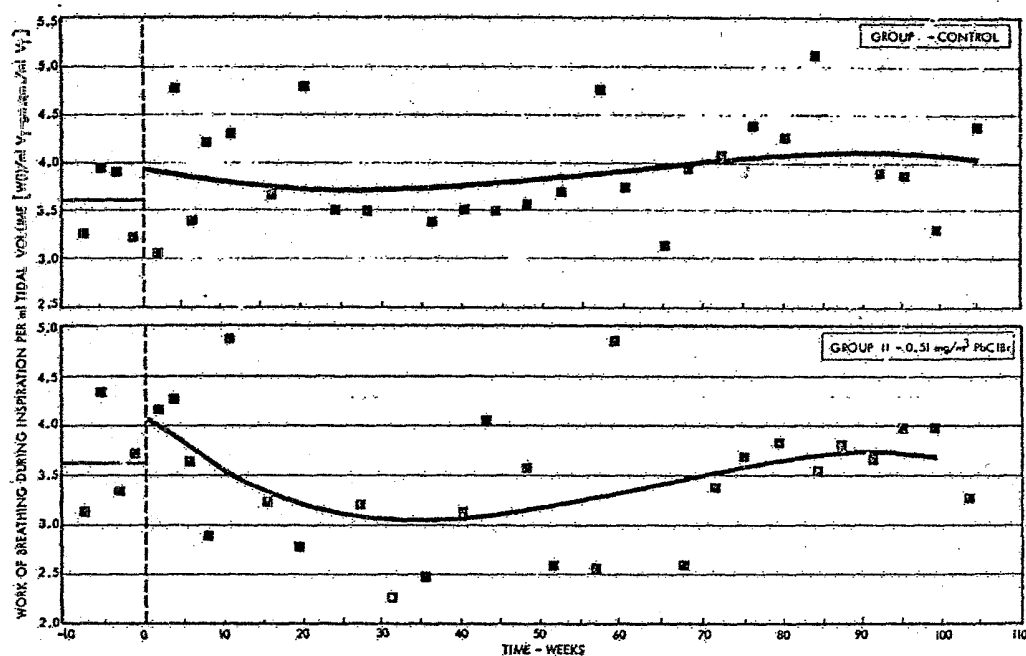


Figure 25 - Third degree polynomial regression curves for $W(i)/ml V_T$ prior to and during exposure to lead chlorobromide. Each point represents the mean for the animals tested at the indicated time for the various groups.

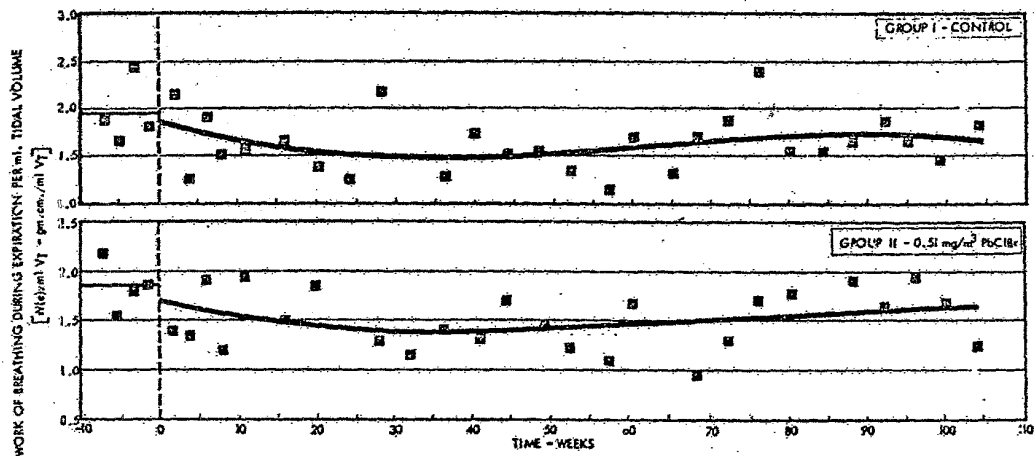


Figure 26 - Third degree polynomial regression curves for $W(e)/ml VT$ prior to and during exposure to lead chlorobromide. Each point represents the mean for the animals tested at the indicated time for the various groups.



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3.3.2. Diffusion

3.3.2.1. Diffusing Capacity of the Lung for Carbon Monoxide (DL_{CO})

Analysis of variance of regression for DL_{CO} (Table 11, Appendix A) revealed no significant slope differences between the two groups. Both groups exhibited an essentially identical increase in DL_{CO} values throughout the experiment, as shown in Figure 27.

3.3.3. Distribution of Inspired Air, Nitrogen Washout

3.3.3.1. Number of Breaths from 80% to 1% Nitrogen [$N(1\% N_2)$]

Analysis of variance of regression for $N(1\% N_2)$ (Table 12, Appendix A) indicated significant differences in the overall mean levels of the groups. Third degree polynomial curves (Figure 28) indicated that both groups followed the same trends with time for $N(1\% N_2)$ values. However, as seen in Figure 28, Group II had somewhat lower pre-exposure values than Group I, but throughout the exposure period, Group II demonstrated higher values than Group I. A t-test for pre-exposure adjusted means of the overall period indicated a significant difference ($t = 4.55$, d.f. = 16).

3.3.3.2. Respiratory Rate Measured During Pure Oxygen Breathing (RR')

Analysis of variance of regression for RR' (Table 13, Appendix A) showed non-parallelism and significant slopes among the groups. The third degree polynomial regression curves (Figure 29) indicated that Group II was similar to Group I until Week 49, after which they deviated somewhat.

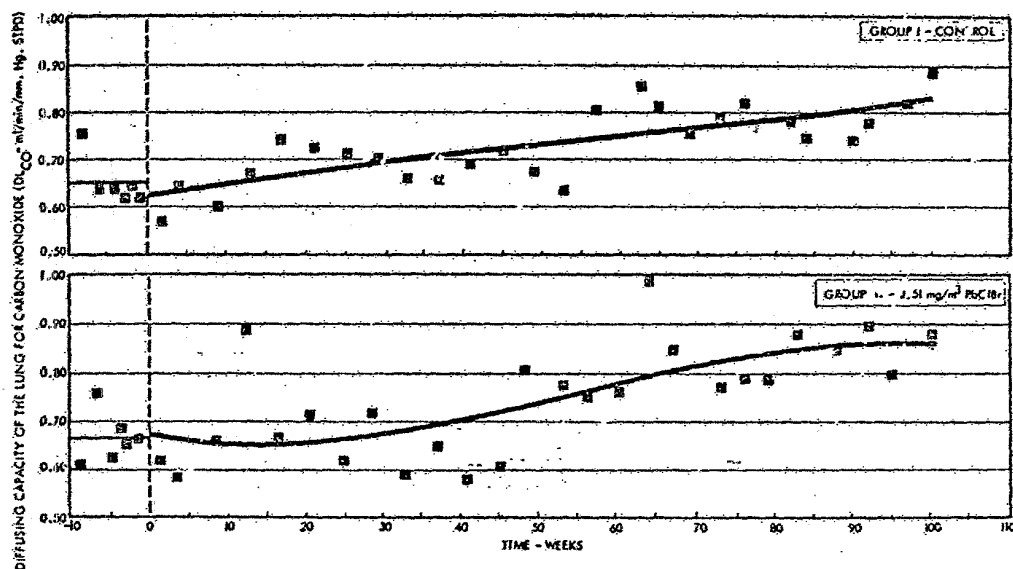


Figure 27 - Third degree polynomial regression curves for DL_{CO} prior to and during exposure to lead chlorobromide. Each point represents the mean for the animals tested at the indicated time for the various groups.

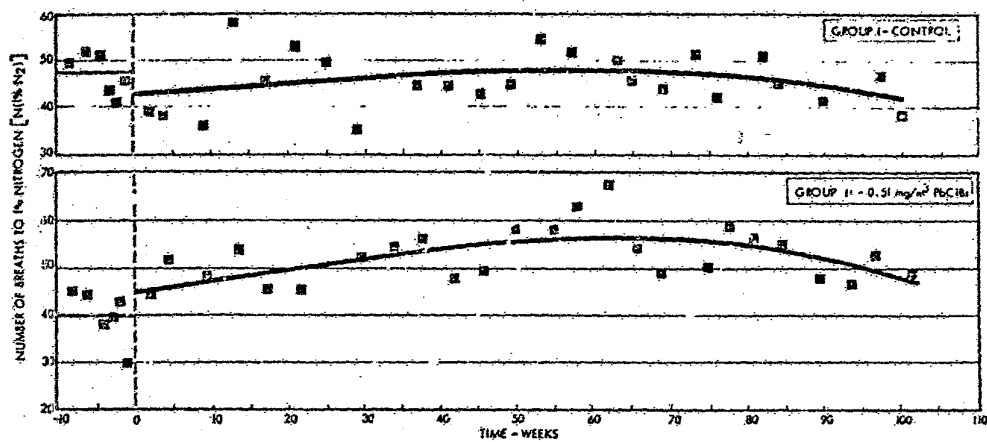


Figure 28 - Third degree polynomial regression curves for N(1% N₂) prior to and during exposure to lead chlorobromide. Each point represents the mean for the animals tested at the indicated time for the various groups.

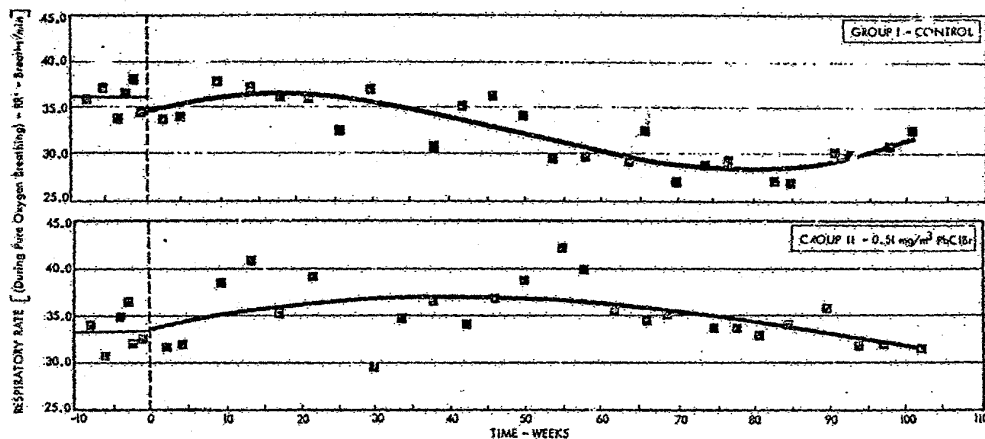


Figure 29 - Third degree polynomial regression curves for RR' prior to and during exposure to lead chlorobromide. Each point represents the mean for the animals tested at the indicated time for the various groups.



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A CUSUM plot of the time-paired differences in the means of the two groups (Figure 30) indicated a change at Week 45, as well as a change from pre-exposure. The two time segments, Weeks 2 through 45 and Weeks 49 through 101, were evaluated by t-tests of the pre-exposure adjusted means which indicated that a small but significant difference between the two groups occurred in the latter exposure segment ($t = 2.94$, d.f. = 16). A similar test of the overall exposure means of these two groups was also significant ($t = 2.61$, d.f. = 16).

3.3.3.3. Cumulative Tidal Volume from 80% to 1% Nitrogen [$CV_T(1\% \text{ N}_2)$]

Analysis of variance of regression for $CV_T(1\% \text{ N}_2)$ (Table 14, Appendix A) indicated no significant slope difference between the groups. The third degree polynomial regression curves (Figure 31) indicated that Group II was slightly higher overall than Group I throughout the exposure period. A t-test of the pre-exposure adjusted overall exposure means comparing these two groups indicated that Group II was significantly higher ($t = 2.24$, d.f. = 13.7) throughout the exposure period.

3.3.3.4. Tidal Volume Measured During Pure Oxygen Breathing (V_T')

Analysis of variance of regression for V_T' (Table 15, Appendix A) measured in the nitrogen washout technique revealed non-parallelism and significant slopes between the groups. The third degree polynomial regression curves are presented in Figure 32.

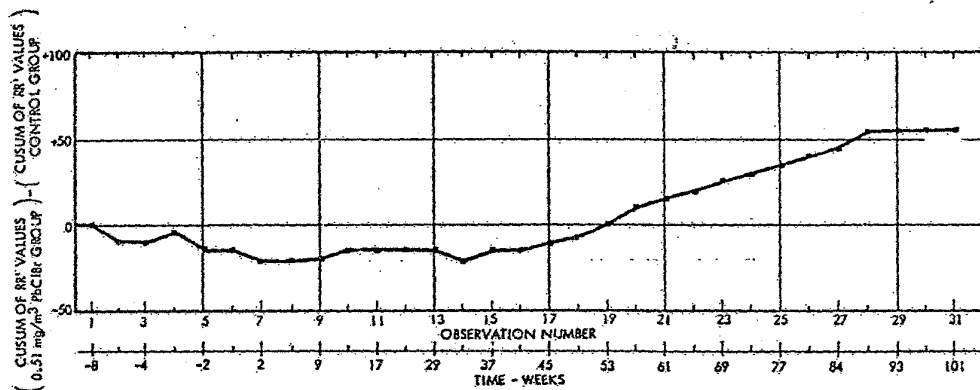


Figure 30 - The time-paired differences between the cumulative sums of RR' between Groups I and II (control and 0.51 mg/m³ PbClBr).

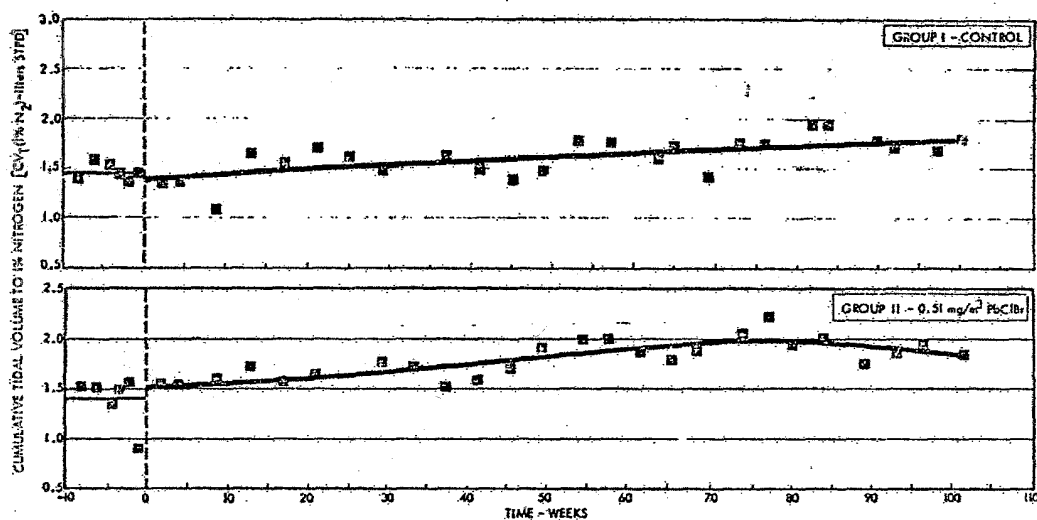


Figure 31 - Third degree polynomial regression curves for CV_T(1% N₂) prior to and during exposure to lead chlorobromide. Each point represents the mean for the animals tested at the indicated time for the various groups.

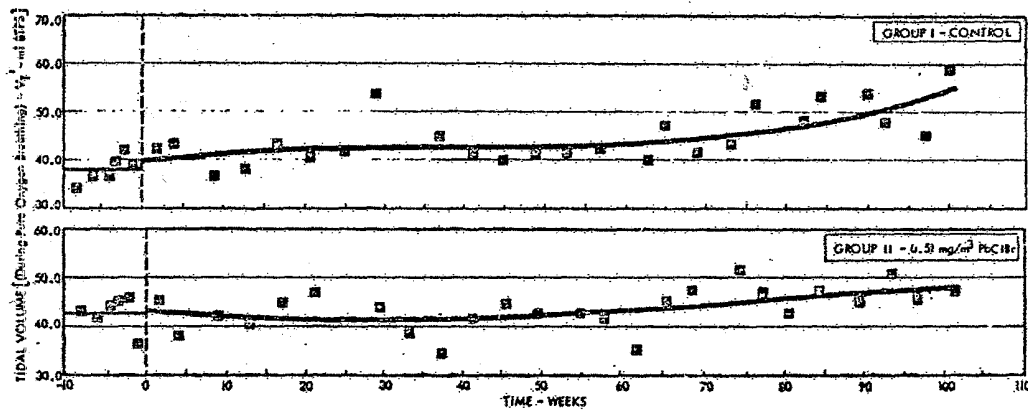


Figure 32 - Third degree polynomial regression curves for V_T prior to and during exposure to lead chlorobromide. Each point represents the mean for the animals tested at the indicated time for the various groups.



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3.4. Hematology

The group means and analysis of variances of the various hematological variables measured are presented in Tables 16, 17, 18, and 19, Appendix A. No consistent trends were noted in any of these variables which remained within normal limits throughout. Random statistically significant differences were seen, but were not consistently related to the exposure conditions.

3.5. Clinical Biochemistry

The group means, standard errors, and the results of the analysis of variance of the various clinical biochemical variables measured are presented in Tables 20 through 33, Appendix A. Scattered statistically significant differences were noted; however, no trends were seen in any of the variables. Throughout the study, the group mean values fluctuated within the normal ranges of these variables.

3.6. Arterial Blood Gas and pH

The group means and standard errors for the blood gas variables are presented in Table 34, Appendix A. Examination of these data did not reveal any consistent trend with time. No apparent exposure-related changes were seen in any of these variables.

3.7. Terminal Body Weight, Organ Weight, and Organ Weight as a Percentage of Body Weight

The data of the terminal body weight, organ weight, and organ/body weight ratios are presented in Tables 35 and 36, Appendix A, for males and females, respectively. Single classification analysis of variance revealed no significant differences between the groups.



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3.8. Histopathology Summary

A detailed listing of the microscopic alterations seen in the the lungs, tracheas, livers, kidneys, peribronchial lymph nodes, and hearts from the animals in the control and exposure groups are found in Table 37, Appendix A. Exposure-related microscopic alterations were seen in the kidneys from the animals exposed to 0.6 mg/m^3 PbClBr . These microscopic alterations were characterized by varying degrees of degeneration in the proximal convoluted tubules. The epithelial cells of the proximal convoluted tubules were slightly vacuolated, and there was also a slight loss of the brush border in some animals. Acid fast intranuclear inclusion bodies were present in the epithelial cells lining the proximal convoluted tubules in seven of the nine animals.

Incidental lesions primarily of an inflammatory nature were seen in the lungs, livers, peribronchial lymph nodes, tracheas, and hearts from the animals in both the control and exposed groups. The incidence and severity of these incidental lesions in the exposed group were comparable to those seen in the control.

3.9. Summary

The inhalation exposure of male and female cynomolgus monkeys to 0.51 mg/m^3 PbClBr resulted in a deterioration in the distribution of ventilation. The number of breaths to 1% nitrogen, cumulative tidal volume to 1% nitrogen, and respiratory rate measured during pure oxygen breathing were significantly elevated in this group. The other physiological parameters measured during exposure were not significantly affected.



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Microscopic alterations related to the exposure to $PbCl_2$ were found in the kidneys of the animals in this group. These histopathological changes were characterized by varying degrees of degeneration of the proximal convoluted tubules. The epithelial cells of the proximal convoluted tubules were slightly vacuolated, possessed irregular luminal borders, and in several areas, had lost their brush border. The nuclei of these epithelial cells were vesiculated and many contained acid fast intranuclear inclusion bodies.

Hematological, clinical biochemical, and arterial blood gas measurements made pre-exposure and periodically throughout the exposure period on the animals in the control and exposed groups did not reveal any meaningful differences. No trends were noted in any of these variables, and, in general, the exposed animals were comparable to the controls. Statistical analysis of the body weights measured periodically throughout the exposure period revealed that all animals in both the control and exposed groups increased in weight with time. No significant differences were detected between the rate of growth in the exposed animals when they were compared with the controls. No significant differences from the controls in terminal body weights, organ weights, and organ/body weight ratios were found for the exposed animals.



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Appendix A - Data compilations and summary of statistical analysis for
Statistical Grouping A, comprised of the following:
Group I - Control and Group II - 0.51 mg/m³ PbClBr.

Table 1 - Monthly means and the grand mean for the analytical concentrations of lead chlorobromide for experimental Group II.

Date	n	$\bar{x}$ mg/m ³	S.D.
5/11/68 - 5/31/68	20	0.8570	1.0552
6/ 1/68 - 6/30/68	30	0.4743	0.6379
7/ 1/68 - 7/31/68	31	0.4565	0.3048
8/ 1/68 - 8/31/68	31	0.6022	0.1088
9/ 1/68 - 9/30/68	30	0.5773	0.1526
10/ 1/68 - 10/31/68	31	0.5074	0.1497
11/ 1/68 - 11/30/68	30	0.4285	0.1944
12/ 1/68 - 12/31/68	31	0.4638	0.1819
1/ 1/69 - 1/31/69	31	0.4752	0.1339
2/ 1/69 - 2/28/69	28	0.6154	0.7173
3/ 1/69 - 3/31/69	31	0.5677	0.1515
4/ 1/69 - 4/30/69	30	0.5147	0.2131
5/ 1/69 - 5/31/69	31	0.7770	0.1710
6/ 1/69 - 6/30/69	30	0.5503	0.1740
7/ 1/69 - 7/31/69	31	0.5597	0.2216
8/ 1/69 - 8/31/69	31	0.5010	0.1545
9/ 1/69 - 9/30/69	30	0.4737	0.2049
10/ 1/69 - 10/31/69	31	0.5352	0.2722
11/ 1/69 - 11/30/69	30	0.4930	0.0363
12/ 1/69 - 12/31/69	31	0.3871	0.1065
1/ 1/70 - 1/31/70	31	0.4052	0.2503
2/ 1/70 - 2/28/70	28	0.5100	0.3669
3/ 1/70 - 3/31/70	31	0.5561	0.2526
4/ 1/70 - 4/30/70	30	0.3070	0.5232
5/ 1/70 - 5/ 5/70	5	0.1080	0.0295

N = 25
 $\bar{X}$ = 0.51
 S.D. = 0.27

Table 2 - Summary of statistical analyses of body weight data for Statistical Grouping A, comprised of the following: Group I - Control and Group II - 0.51 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	1	1.689 x 10 ⁻¹	1.689 x 10 ⁻¹	0.13	-
Error Deviation	479	6.257 x 10 ⁻²	1.306	-	-

FIRST DEGREE POLYNOMIAL REGRESSION COEFFICIENTS					
GROUPS	REGRESSION COEFFICIENTS		S.E.		
	A	B			
I	2.63 ± 0.052	1.64 x 10 ⁻² ± 8.93 x 10 ⁻⁴	Sy.x	n	r
II	2.61 ± 0.46	1.53 x 10 ⁻² ± 8.02 x 10 ⁻⁴	0.14	33	0.96
			0.13	33	0.97

Table 3 - Summary of statistical analyses of total respiratory system flow resistance during inspiration data for Statistical Grouping A, comprised of the following: Group I - Control and Group II - 0.51 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	1	2.963 x 10 ⁻⁴	2.963 x 10 ⁻⁴	2.12	-
Error Deviation	586	8.175 x 10 ⁻²	1.395 x 10 ⁻⁴	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.					n	r
	A	B	C	D	Sy.x		
I	0.044 ± 0.0033	2.12 x 10 ⁻⁴ ± 3.81 x 10 ⁻⁴	-9.72 x 10 ⁻⁶ ± 9.30 x 10 ⁻⁶	8.10 x 10 ⁻⁸ ± 6.10 x 10 ⁻⁸	0.008	39	0.27
II	0.053 ± 0.0026	-5.52 x 10 ⁻⁴ ± 3.01 x 10 ⁻⁴	5.42 x 10 ⁻⁶ ± 7.35 x 10 ⁻⁶	-2.00 x 10 ⁻⁹ ± 4.80 x 10 ⁻⁸	0.006	39	0.65

Table 4 - Summary of statistical analyses of total respiratory system flow resistance during expiration data for Statistical Grouping A, comprised of the following: Group I - Control and Group II 0.51 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	1	2.580 x 10 ⁻⁵	2.580 x 10 ⁻⁵	0.24	-
Error Deviation	586	6.304 x 10 ⁻²	1.076 x 10 ⁻⁴	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS						
GROUPS	REGRESSION COEFFICIENTS ± S.E.					
	A	B	C	D	Sy.x	r
I	0.042 ± 0.0028	-2.07 x 10 ⁻⁴ ± 3.26 x 10 ⁻⁴	-1.34 x 10 ⁻⁶ ± 7.97 x 10 ⁻⁶	2.90 x 10 ⁻⁸ ± 5.20 x 10 ⁻⁸	0.006	0.55
II	0.046 ± 0.0023	-6.02 x 10 ⁻⁴ ± 2.70 x 10 ⁻⁴	7.30 x 10 ⁻⁶ ± 6.61 x 10 ⁻⁶	-1.90 x 10 ⁻⁸ ± 4.30 x 10 ⁻⁸	0.005	0.67

Table 5 - Summary of statistical analyses of tidal volume data for Statistical Grouping A, comprised of the following: Group I - Control and Group II - 0.51 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p $\leq$.05
Non-Parallelism	1	4.771	4.771	0.03	-
Error Deviation	462	6.649×10^4	1.439×10^2	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS $\pm$ S.E.					n	r
	A	B	C	D	SV.X		
I	28.72 ± 1.92	2.52×10^{-1} $\pm 1.88 \times 10^{-1}$	-2.46×10^{-3} $\pm 4.42 \times 10^{-3}$	1.16×10^{-5} $\pm 2.84 \times 10^{-5}$	3.48	32	0.77
II	31.10 ± 1.75	1.64×10^{-2} $\pm 1.72 \times 10^{-1}$	5.87×10^{-4} $\pm 4.10 \times 10^{-3}$	3.80×10^{-6} $\pm 2.64 \times 10^{-5}$	3.20	31	0.79

Table 6 - Summary of statistical analyses of respiratory rate for Statistical Grouping A, comprised of the following: Group I - Control and Group II - 0.51 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	1	7.443 x 10 ²	7.443 x 10 ²	10.60	Yes
Error Deviation	462	3.243 x 10 ⁴	7.020 x 10 ¹	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS						
GROUPS	REGRESSION COEFFICIENTS ± S.E.				SV, %	r
	A	B	C	D		
I	40.74 ± 1.26	3.16×10^{-1} ± 1.23 × 10 ⁻¹	-9.30×10^{-3} ± 2.90 × 10 ⁻³	5.63×10^{-5} ± 1.86 × 10 ⁻⁵	2.29	0.84
II	37.85 ± 1.83	2.67×10^{-1} ± 1.80 × 10 ⁻¹	-4.08×10^{-3} ± 4.28 × 10 ⁻³	1.39×10^{-5} ± 2.76 × 10 ⁻⁵	3.34	0.51

Table 7 - Summary of statistical analyses of dynamic compliance of the lung data for Statistical Grouping A, comprised of the following: Group I - Control and Group II - 0.51 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	1	6.535×10^{-1}	6.535×10^{-1}	0.12	-
Error Deviation	462	2.397×10^3	5.188	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.				SV, X	n	r
	A	B	C	D			
I	6.01 ± 0.46	1.83×10^{-2} ± 4.55×10^{-2}	-1.88×10^{-4} ± 1.07×10^{-3}	1.30×10^{-6} ± 6.90×10^{-6}	0.84	32	0.43
II	6.09 ± 0.57	6.22×10^{-2} ± 5.65×10^{-2}	-1.12×10^{-3} ± 1.34×10^{-3}	6.80×10^{-6} ± 8.70×10^{-6}	1.05	31	0.45

Table 8 - Summary of statistical analyses of pulmonary flow resistance data for Statistical Grouping A, comprised of the following: Group I - Control and Group II - 0.51 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION						
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05	
Non-Parallelism	1	1.094×10^{-3}	1.094×10^{-3}	6.99	Yes	
Error Deviation	462	7.232×10^{-2}	1.565×10^{-4}	-	-	

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS						
GROUPS	REGRESSION COEFFICIENTS ± S.E.			Sy.x	n	r
	A	B	C			
I	0.024 ± 0.0036	7.84×10^{-5} $\pm 3.53 \times 10^{-4}$	8.71×10^{-7} $\pm 8.32 \times 10^{-6}$	-1.80×10^{-8} $\pm 5.30 \times 10^{-8}$	0.006	32
II	0.025 ± 0.0039	8.93×10^{-6} $\pm 3.82 \times 10^{-4}$	-7.73×10^{-7} $\pm 9.10 \times 10^{-6}$	-3.00×10^{-9} $\pm 5.90 \times 10^{-8}$	0.007	31

Table 9 - Summary of statistical analyses of work of breathing during inspiration per ml tidal volume data for Statistical Grouping A, comprised of the following: Group I - Control and Group II - 0.51 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	1	2.500	2.500	1.56	-
Error Deviation	462	7.403×10^2	1.602	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.				SY.X	n	r
	A	B	C	D			
I	3.94 ± 0.30	-2.00×10^{-2} ± 2.97×10^{-2}	5.07×10^{-4} ± 7.00×10^{-4}	-2.90×10^{-6} ± 4.50×10^{-6}	0.55	32	0.25
II	4.13 ± 0.36	-7.58×10^{-2} ± 3.54×10^{-2}	1.49×10^{-3} ± 8.43×10^{-4}	-7.90×10^{-6} ± 5.40×10^{-6}	0.66	31	0.46

Table 10 - Summary of statistical analyses of work of breathing during expiration per ml tidal volume data for Statistical Grouping A, comprised of the following: Group I - Control and Group II - 0.5l mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	1	5.977×10^{-2}	5.977×10^{-2}	0.17	-
Error Deviation	462	1.592×10^2	3.447×10^{-1}	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS					
GROUPS	REGRESSION COEFFICIENTS ± S.E.				
	A	B	C	D	SV.X
I	1.85 ± 0.16	$-2.66 \times 10^{-2} \pm 1.60 \times 10^{-2}$	$5.48 \times 10^{-4} \pm 3.76 \times 10^{-4}$	$-3.00 \times 10^{-6} \pm 2.40 \times 10^{-6}$	0.30
II	1.73 ± 0.16	$-2.15 \times 10^{-2} \pm 1.57 \times 10^{-2}$	$3.97 \times 10^{-4} \pm 3.74 \times 10^{-4}$	$-1.80 \times 10^{-6} \pm 2.40 \times 10^{-6}$	0.29
					0.36
					0.39

Table 11 - Summary of statistical analyses of diffusing capacity of the lung for carbon monoxide data for Statistical Grouping A, comprised of the following: Group I - Control and Group II - 0.51 mg/m³ pClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	1	1.448×10^{-2}	1.448×10^{-2}	0.54	-
Error deviation	479	1.276×10^1	2.663×10^{-2}	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS					
GROUPS	REGRESSION COEFFICIENTS ± S.E.				
	A	B	C	D	r
I	0.62 ± 0.031	3.04×10^{-3} $\pm 2.91 \times 10^{-3}$	-2.49×10^{-5} $\pm 7.00 \times 10^{-5}$	1.50×10^{-7} $\pm 4.60 \times 10^{-7}$	0.78
II	0.67 ± 0.052	-3.37×10^{-3} $\pm 4.83 \times 10^{-3}$	1.26×10^{-4} $\pm 1.16 \times 10^{-4}$	-7.50×10^{-7} $\pm 7.70 \times 10^{-7}$	0.68

Table 12 - Summary of statistical analyses of number of breaths to 1% nitrogen data for Statistical Grouping A, comprised of the following: Group I - Control and Group II - 0.51 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	1	3.352 x 10 ²	3.352 x 10 ²	1.87	-
Error Deviation	464	8.337 x 10 ⁴	1.797 x 10 ²	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS					
GROUPS	REGRESSION COEFFICIENTS ± S.E.				
	A	B	C	D	r
I	42.85 ± 3.42	8.85 x 10 ⁻² ± 3.26 x 10 ⁻¹	1.08 x 10 ⁻³ ± 3.26 x 10 ⁻³	2.10 x 10 ⁻⁵ ± 5.20 x 10 ⁻⁵	0.33
II	44.77 ± 3.08	2.51 x 10 ⁻¹ ± 2.93 x 10 ⁻¹	1.16 x 10 ⁻³ ± 7.06 x 10 ⁻³	-3.40 x 10 ⁻⁵ ± 4.70 x 10 ⁻⁵	0.64

Table 13 - Summary of statistical analyses of respiratory rate (during oxygen breathing) data for Statistical Grouping A, comprised of the following: Group I - Control and Group II - 0.51 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION						
SOURCE OF VARIATION	df	SS	MS	F	p	$\leq .05$
Non-Parallelism	1	3.722×10^2	3.722×10^2	5.04	Yes	
Error Deviation	464	3.427×10^4	7.386×10^1	-	-	

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS						
GROUPS	REGRESSION COEFFICIENTS $\pm$ S.E.					
	A	B	C	D	SY.X	r
I	34.46 ± 1.11	2.49×10^{-1} $\pm 1.06 \times 10^{-1}$	-9.27×10^{-3} $\pm 2.54 \times 10^{-3}$	-9.27×10^{-5} $\pm 2.54 \times 10^{-5}$	1.84	0.86
II	33.38 ± 1.80	1.91×10^{-1} $\pm 1.71 \times 10^{-1}$	-2.86×10^{-3} $\pm 4.13 \times 10^{-3}$	7.40×10^{-6} $\pm 2.72 \times 10^{-6}$	3.02	0.52

Table 14 - Summary of statistical analyses of cumulative tidal volume to 1% nitrogen data for Statistical Grouping A, comprised of the following: Group I - Control and Group II - 0.51 mg/m³ PBClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	1	7.581×10^{-3}	7.581×10^{-3}	0.04	-
Error Deviation	464	8.287×10^1	1.786×10^{-1}	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS						
GROUPS	REGRESSION COEFFICIENTS ± S.E.					
	A	B	C	D	Sy.x	r
I	1.35 ± 0.094	5.79×10^{-3} $\pm 8.95 \times 10^{-3}$	-1.38×10^{-5} $\pm 2.15 \times 10^{-4}$	0.00 $\pm 1.40 \times 10^{-6}$	0.16	0.70
II	1.52 ± 0.074	4.55×10^{-4} $\pm 7.05 \times 10^{-3}$	2.09×10^{-4} $\pm 1.70 \times 10^{-4}$	-1.80×10^{-6} $\pm 1.10 \times 10^{-6}$	0.12	0.82

Table 15 - Summary of statistical analyses of tidal volume (during oxygen breathing) data for Statistical Grouping A, comprised of the following: Group I - Control and Group II - 0.51 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p < .05
Non-Parallelism	1	3.850 x 10 ²	3.850 x 10 ²	3.43	
Error Deviation	464	5.211 x 10 ⁴	1.123 x 10 ²	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS					
GROUPS	REGRESSION COEFFICIENTS ± S.E.			Sv.x	n
	A	B	C		
I	39.08 ± 2.58	2.20 x 10 ⁻¹ ± 2.47 x 10 ⁻¹	-5.34 x 10 ⁻³ ± 5.92 x 10 ⁻³	4.30	32
			4.68 x 10 ⁻⁵ ± 3.91 x 10 ⁻⁵		
II	43.09 ± 2.17	-1.77 x 10 ⁻¹ ± 2.07 x 10 ⁻¹	3.84 x 10 ⁻³ ± 4.97 x 10 ⁻³	3.64	32
			-1.63 x 10 ⁻⁵ ± 3.28 x 10 ⁻⁵		
				0.70	0.53

Table 16 - Mean values $\pm$ (S.E.) and summary of single classification analysis of variance for hematocrit (Hct. - percent) for male and female monkeys in Statistical Grouping A.

Groups	Time-Weeks						
	Pre-exposure	-8	4	16	40	68	104
I - Control		36.4 (0.8)	36.0 (1.0)	33.1 (1.0)	35.4 (0.8)	37.3 (1.0)	36.7 (0.8)
II - 0.51 mg/m ³ PbClBr		32.3 (0.8)	35.8 (0.8)	34.3 (0.9)	33.5 (0.9)	35.4 (1.1)	36.2 (0.9)

Comparison of Experimental Treatment Effects ($p \leq 0.05$)

Groups	Time-Weeks						
	Pre-exposure	-8	4	16	40	68	104
I vs II	SIG		N.S.	N.S.	N.S.	N.S.	N.S.

Table 17 - Mean values $\pm$ (S.E.) and summary of single classification analysis of variance for hemoglobin (Hgb. - grams percent) for male and female monkeys in Statistical Grouping A.

Groups	Time-Weeks						
	Pre-exposure	-8	4	16	40	68	104
I - Control	10.5 (0.3)		11.0 (0.3)	11.2 (0.2)	10.9 (0.3)	10.7 (0.3)	11.7 (0.3)
II - 0.51 mg/m ³ PbClBr	10.2 (0.2)		9.8 (0.2)	10.4 (0.2)	9.1 (0.2)	10.4 (0.3)	10.6 (0.3)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Groups	Time-Weeks						
	Pre-exposure	-8	4	16	40	68	104
I vs II	N.S.		SIG	SIG	SIG	N.S.	SIG

Table 18 - Mean values $\pm$ (S.E.) and summary of single classification analysis of variance for total erythrocyte count (RBC $\sim$ 106/cmm) for male and female monkeys in Statistical Grouping A.

Groups	Time-Weeks			
	Pre-exposure -8	4	16	40 68 104
I - Control	5.43 (0.09)	5.44 (0.18)	5.69 (0.22)	5.29 (0.18) 5.10 (0.14) 6.12 (0.15)
II - 0.51 mg/m ³ PbClBr	5.12 (0.18)	4.89 (0.21)	5.38 (0.30)	5.19 (0.19) 5.64 (0.23) 5.80 (0.19)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Groups	Time-Weeks			
	Pre-exposure -8	4	16	40 68 104
I vs II	N.S.	N.S.	N.S.	N.S. N.S. N.S.

Table 19 - Mean values $\pm$ (S.E.) and summary of single classification analysis of variance for total leukocyte count (WBC - per cmm) for male and female monkeys in Statistical Grouping A.

Groups	Time-Weeks				
	Pre-exposure -8	4 *	16	40	68
I - Control	7244 (844)	7171 (299)	8678 (716)	10622 (853)	8222 (687)
II - 0.51 mg/m ³ PbClBr	8433 (863)	11044 (3068)	9699 (932)	8867 (837)	9111 (854)
					11944 (1113)
					9422 (872)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Groups	Time-Weeks				
	Pre-exposure -8	4	16	40	68
I vs II	N.S.	N.S.	N.S.	N.S.	N.S.
					SIG

* The variances of these groups were heterogeneous.

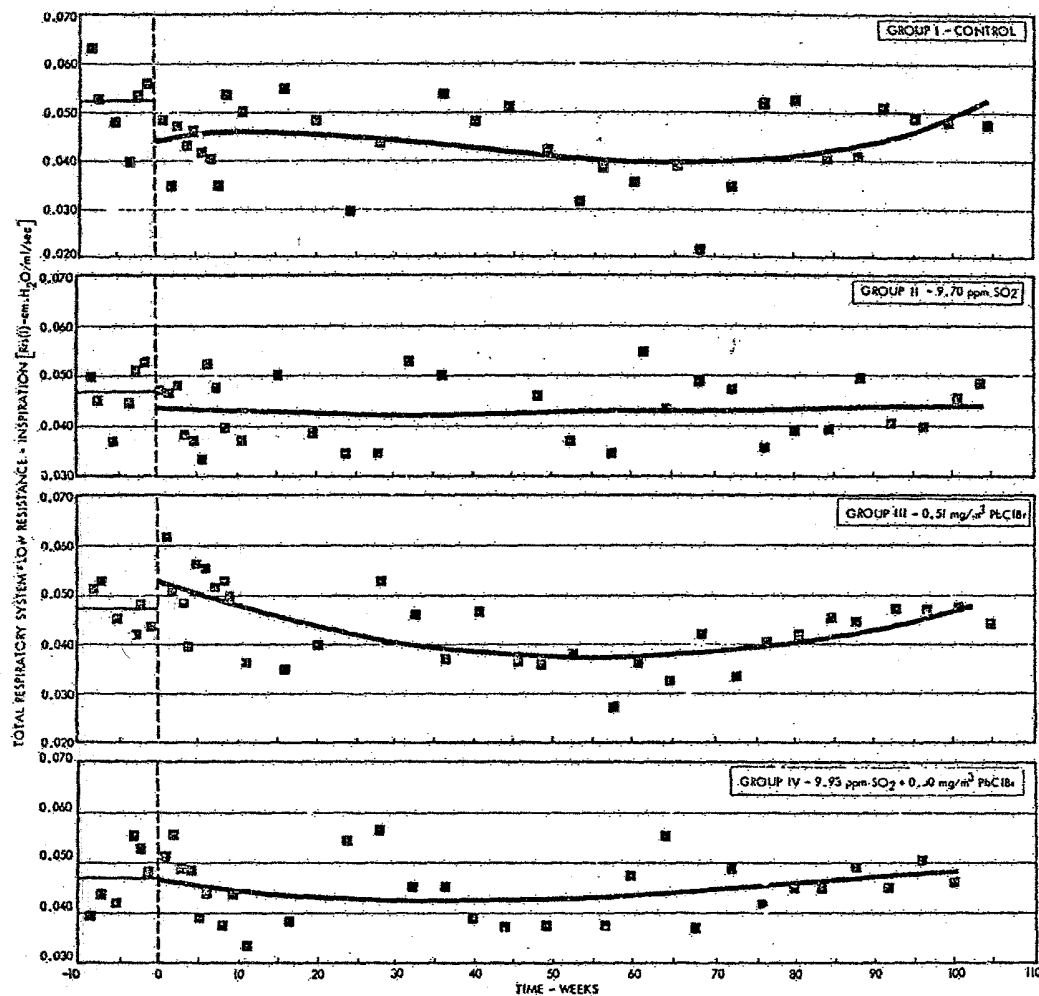


Figure 53 - Third degree polynomial regression curves for $R_{rs}(i)$ prior to and during exposure to sulfur dioxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.

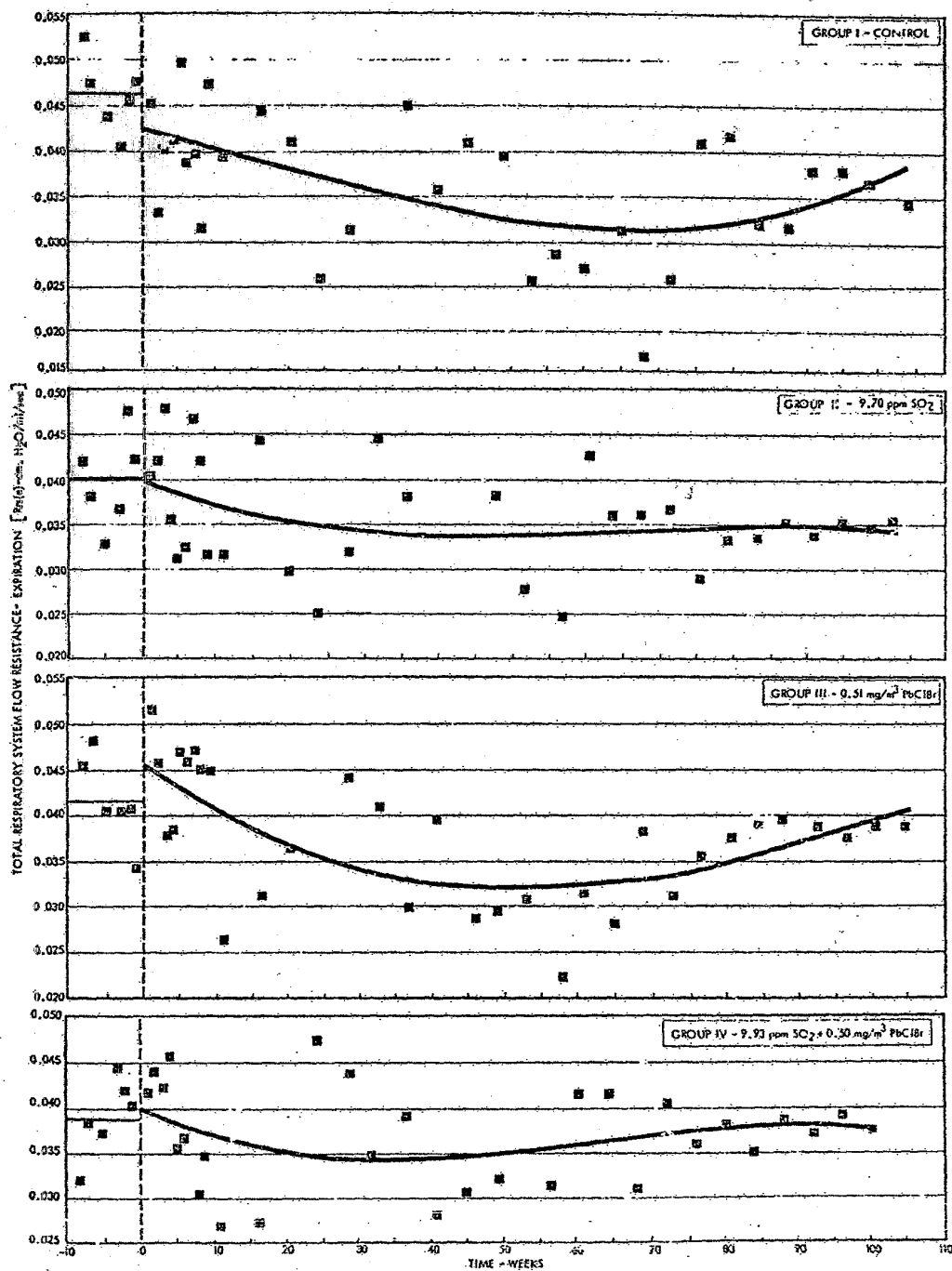


Figure 54- Third degree polynomial regression curves for Rrs(e) prior to and during exposure to sulfur dioxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.

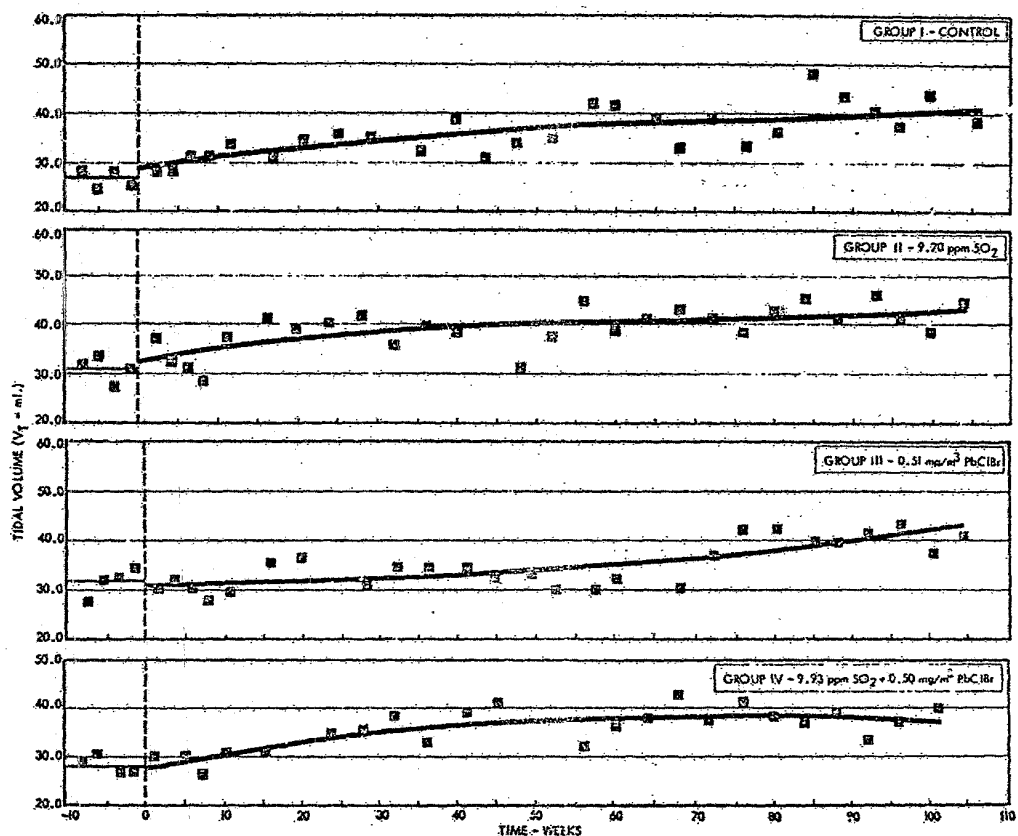


Figure 55 - Third degree polynomial regression curves for V_T prior to and during exposure to sulfur dioxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.



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3.3.1.4. Respiratory Rate (RR)

Analysis of variance of regression for RR (Table 8, Appendix C) indicated non-parallelism among the groups. The third degree polynomial regression curves are shown in Figure 56. Inspection of Figure 56 indicated that RR values for Group IV were slightly higher during the pre-exposure period and remained slightly higher throughout the exposure period.

3.3.1.5. Dynamic compliance of the Lung [Cdyn(1)]

Analysis of variance of regression for Cdyn(1) (Table 9, Appendix C) revealed non-parallelism among the groups. The third degree polynomial regression curves are shown in Figure 57. Inspection of Figure 57 shows that Group I, which was considerably lower in Cdyn(1) during the pre-exposure period, had a marked increase at the start of the "exposure" period and increased slightly thereafter as did Groups III and IV. Group II, on the other hand, started from a higher pre-exposure level, increased at the start of exposure but did not increase further. The difference between the pre-exposure adjusted overall means of Groups I and II was not significant ($t = 1.87$, d.f. = 15). The pre-exposure adjusted differences in the means of the first year for Group I vs. Group III and for Group I vs. Group IV were significant ($t = 2.69$, d.f. = 16 and $t = 2.30$, d.f. = 16, respectively); however, the large jump between the pre-exposure values and the start of the "exposure" period in Group I renders difficult any interpretation of these differences.

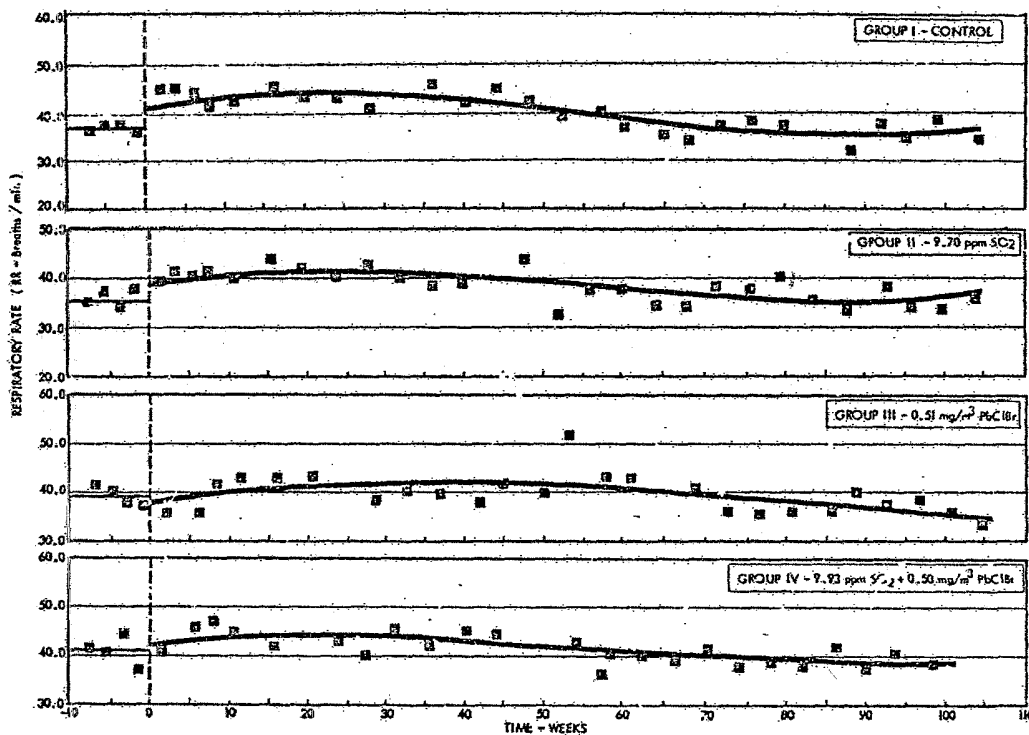


Figure 56 - Third degree polynomial regression curves for RR prior to and during exposure to sulfur dioxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.

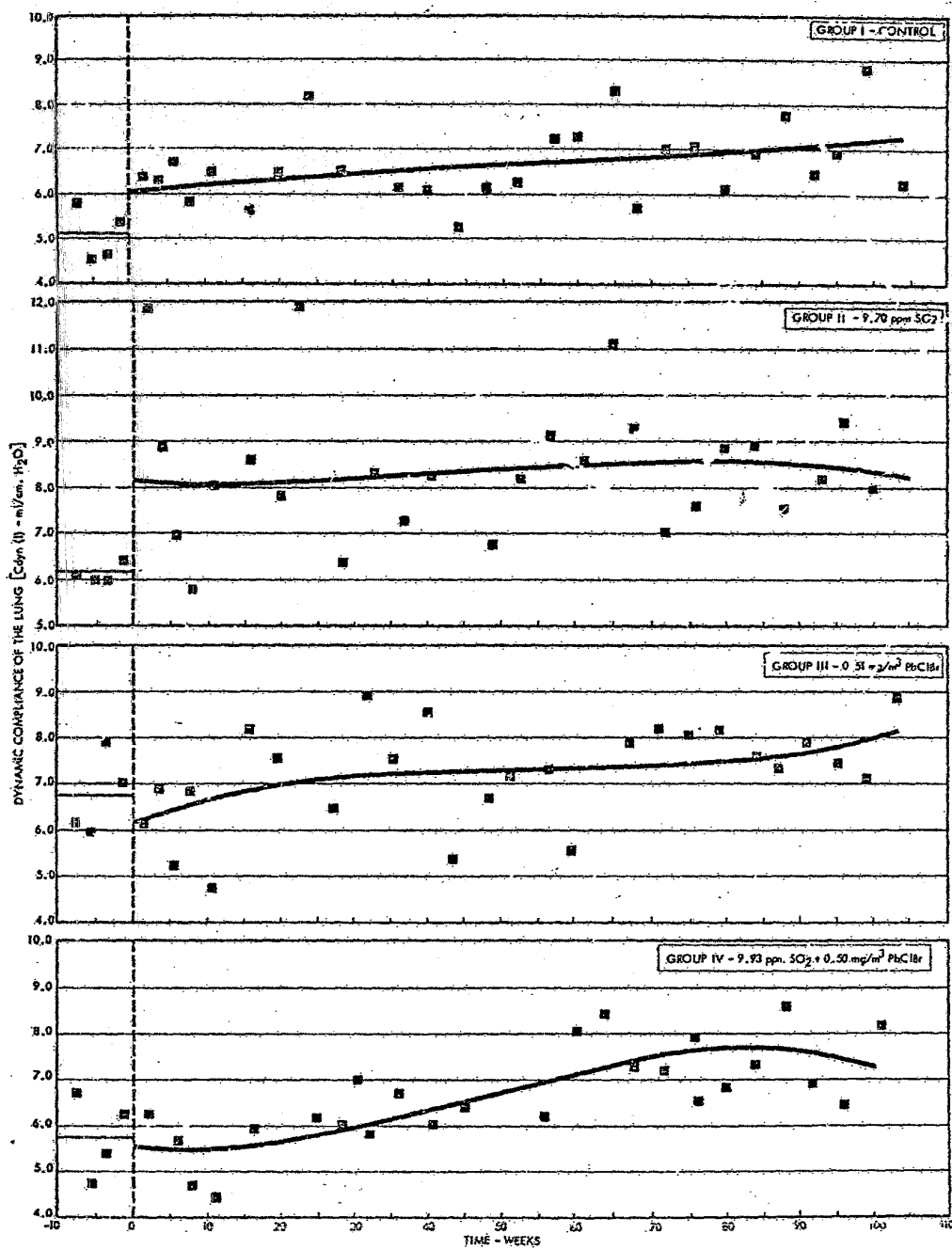


Figure 57 - Third degree polynomial regression curves for Cdyn(I) prior to and during exposure to sulfur dioxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.



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3.3.1.6. Pulmonary Flow Resistance (R_l)

Analysis of variance of regression for R_l (Table 10, Appendix C) indicated non-parallelism among the groups. The third degree polynomial regression curves are presented in Figure 58. Inspection of this Figure indicates that the trends with time differed among the groups, but that the R_l values were generally similar for all groups, except Group I, which did not decrease as much with time. A t-test of the pre-exposure adjusted means of the first nine weeks of exposure indicated that Group IV was significantly higher than Group I ($t = 2.39$, d.f. = 16) as was Group III ($t = 2.66$, d.f. = 16).

3.3.1.7. Work of Breathing During Inspiration per ml Tidal Volume [$W(i)/ml V_T$]

Analysis of variance of regression for $W(i)/ml V_T$ (Table 11, Appendix C) revealed non-parallelism among the groups. The third degree polynomial regression curves are presented in Figure 59. Inspection of this Figure indicates that both Groups III and IV had lower values than Group I throughout the study.

3.3.1.8. Work of Breathing During Expiration per ml Tidal Volume [$W(e)/ml V_T$]

Analysis of variance of regression for $W(e)/ml V_T$ (Table 12, Appendix C) indicated no significant slope differences among the groups. The third degree polynomial regression curves (Figure 60) also indicated no observable differences among the groups.

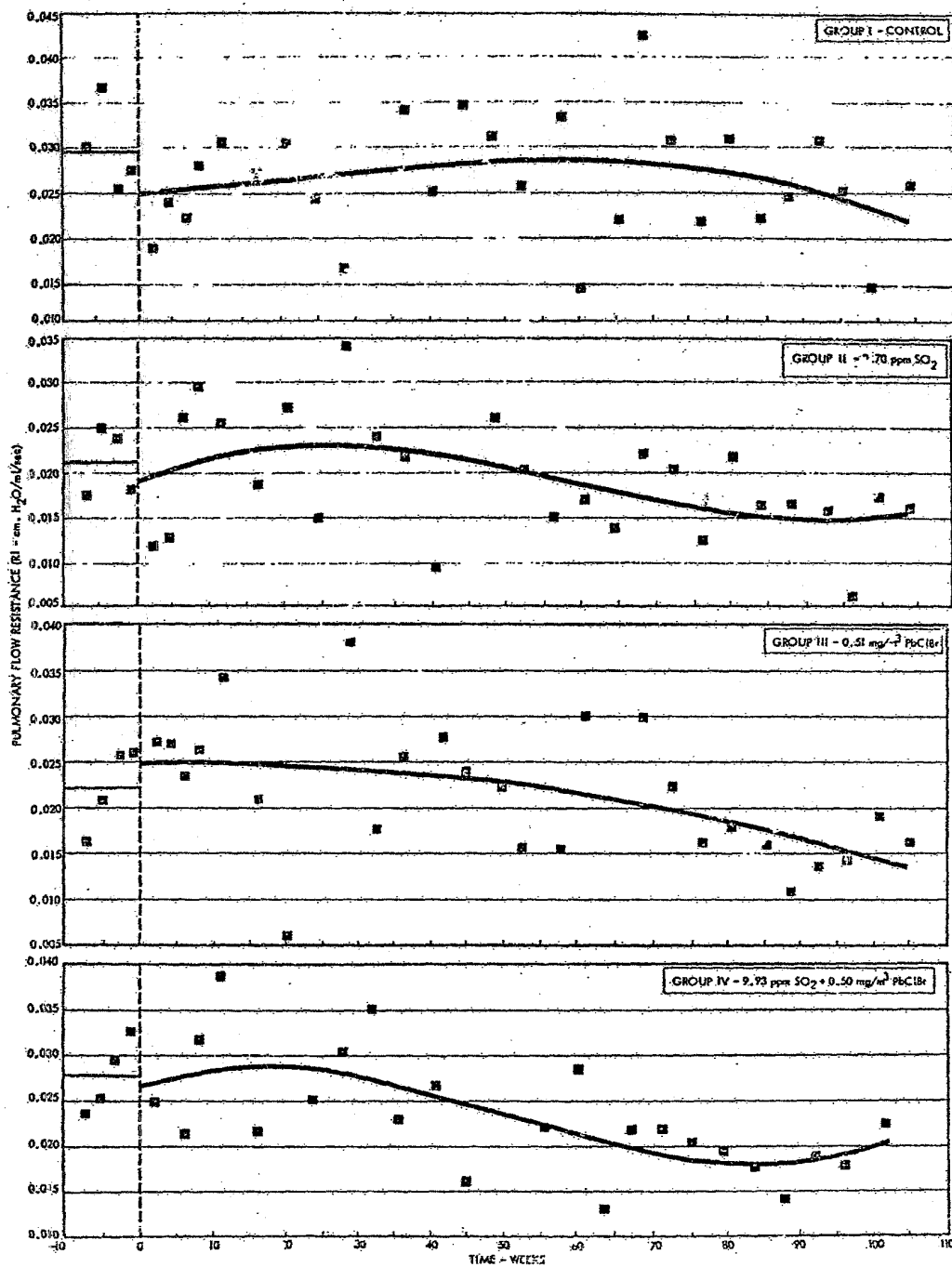


Figure 58 - Third degree polynomial regression curves for Rl prior to and during exposure to sulfur dioxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.

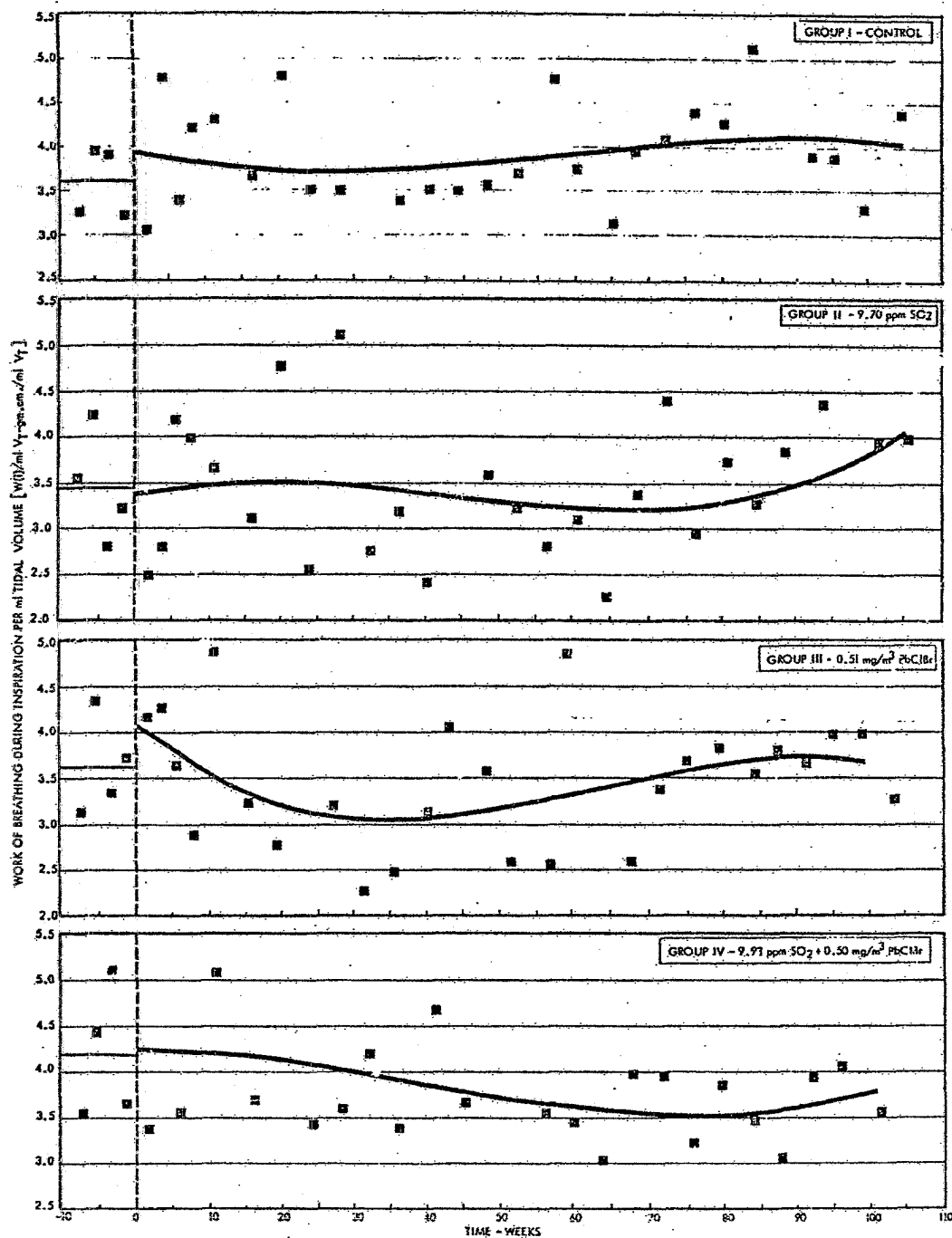


Figure 59 - Third degree polynomial regression curves for $W(i)/ml V_T$ prior to and during exposure to sulfur dioxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.

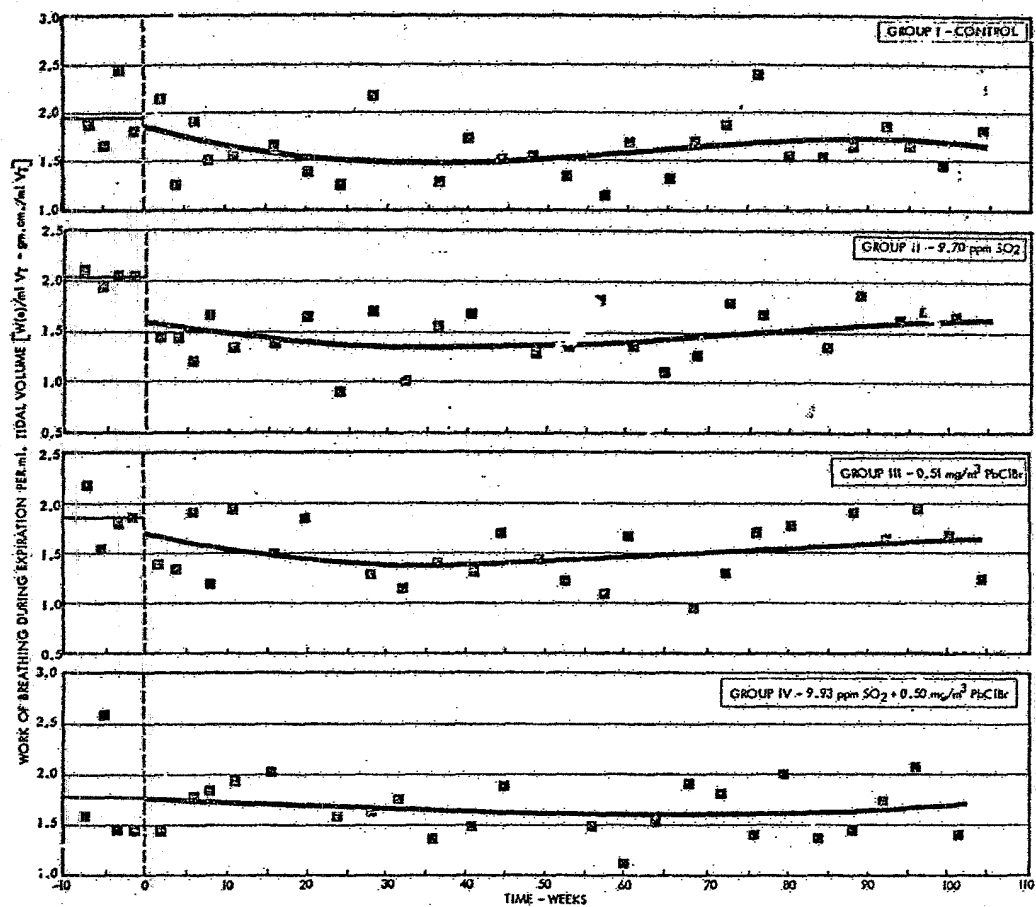


Figure 60 - Third degree polynomial regression curves for $W(e)/ml V_T$ prior to and during exposure to sulfur dioxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.



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3.3.2. Diffusion

3.3.2.1. Diffusing Capacity of the Lung for Carbon Monoxide (DL_{CO})

Analysis of variance of regression for DL_{CO} (Table 13, Appendix C) revealed no significant slope differences among the groups. The third degree polynomial regression curves (Figure 61) indicated that DL_{CO} for all groups increased with time.

3.3.3. Distribution of Inspired Air, Nitrogen Washout

3.3.3.1. Number of Breaths from 80% t , 1% Nitrogen [$N(1\% N_2)$]

Analysis of variance of regression for $N(1\% N_2)$ (Table 14, Appendix C) indicated no significant slope differences among the groups. Inspection of the third degree polynomial regression curves (Figure 62), indicated that $N(1\% N_2)$ values for Group I were somewhat higher during the pre-exposure control period than value for Groups II, III, and IV. During the entire exposure period, $N(1\% N_2)$ values for Groups I and II were similar, but values for Groups III and IV were at a higher level. Separate t-tests of the pre-exposure adjusted overall exposure means were made to compare Group I with Groups II, III, and IV during the exposure period. These tests indicated that Groups II, III, and IV were each significantly higher than Group I ($t = 2.77$, d.f. = 16; $t = 4.55$, d.f. = 16; and $t = 3.26$, d.f. = 16, respectively).

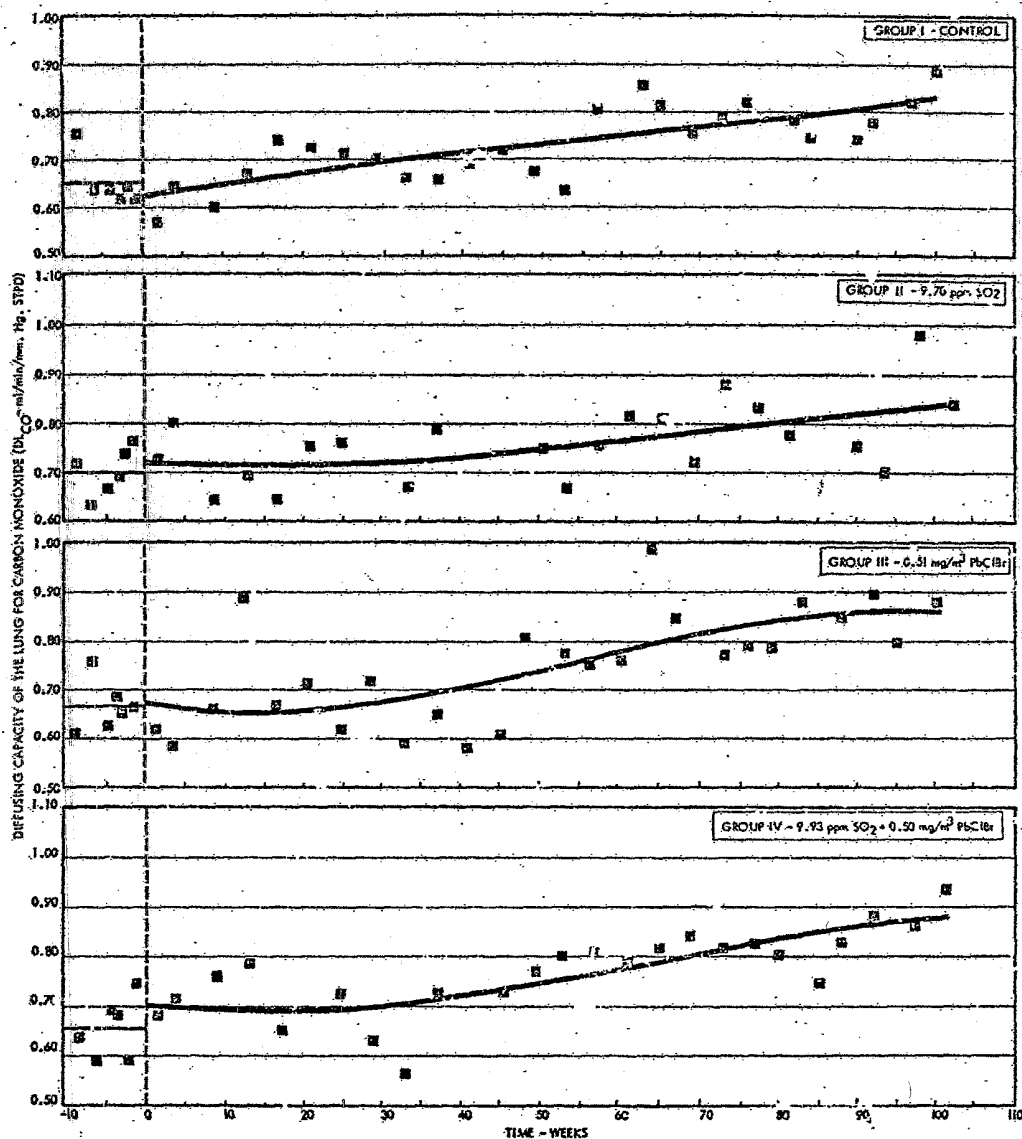


Figure 61 - Third degree polynomial regression curves for DLCO prior to and during exposure to sulfur dioxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.

Table 37 - Continued

	GROUPS	
	<u>I</u>	<u>II</u>
KIDNEY		
Interstitial Nephritis	0/9	2/9
Epithelial Vacuolation	1/9	3/9
Tubular Dilatation	3/9	0/9
Loss of the Brush Border	0/9	3/9
Nuclear Vesiculation	0/9	0/9
Tubular Hypertrophy	0/9	0/9
Pyelitis	0/9	0/9
Focal Mineralization	0/9	1/9
Glomerular Degeneration	0/9	0/9
Inclusion Bodies	0/9	7/9
Vasculitis	0/9	0/9
Congestion	0/9	0/9
Focal Fibrosis	0/9	0/9
Perirenal Abscess	0/9	0/9
Protein Inhibition	0/9	1/9
Intima Thickening	0/9	0/9
Endothelial Hyperplasia	0/9	0/9
HEART		
Focal Myocarditis	3/9	0/9
Endocarditis	0/9	0/9
Epicarditis	0/9	0/9
Myocardial Degeneration	1/9	0/9
Vasculitis	0/9	0/9
Subendocardial Hemorrhage	0/9	0/9
Thickened Endocardium	0/9	0/9
Focal Hyperplasia in the Endothelium	0/9	0/9
Intima Thickening	0/9	0/9
Granular Pigment	0/9	0/9



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IV. STATISTICAL GROUPING B - RESULTS OF THE CHRONIC EXPOSURE OF CYNOMOLGUS MONKEYS TO 0.51 PPM NITROGEN DIOXIDE (NO_2), 0.51 MG/M^3 LEAD CHLOROBROMIDE (PbClBr), AND 0.48 PPM NO_2 COMBINED WITH 0.54 MG/M^3 PbClBr

Four groups of animals comprised the second statistical grouping - B. One group was maintained as the control group exposed to filtered room air, one group was exposed to nitrogen dioxide alone, one group was exposed to lead chlorobromide alone, and one group was exposed to nitrogen dioxide and lead chlorobromide in binary combination. Group designations used throughout this section are presented in Table 11.

Table 11 - Group B designations

<u>Group Designation (No.)</u>	<u>Agent</u>	<u>Nominal Concentration</u>	<u>Mean Analytical Concentration</u>
I (1)	Control	0	0
II (2)	NO_2	0.50 ppm	0.51 ppm
III (9)	PbClBr	0.60 mg/m^3	0.51 mg/m^3
IV (10)	NO_2	0.50 ppm	0.48 ppm
	PbClBr	0.60 mg/m^3	0.54 mg/m^3

1. Exposure Concentrations

The chamber concentrations for Groups II, III, and IV as determined analytically throughout the study are presented in Tables 1, 2, and 3, Appendix B. The mean and standard deviation for the group exposed to NO_2 alone after 87 weeks of exposure was 0.51 ppm $\pm$ 0.06. The mean and standard deviation for the group exposed to PbClBr alone after 104 weeks of exposure was 0.51 mg/m^3 $\pm$ 0.27, and for the group exposed to the combination of these two materials, means, and standard deviations were 0.48 ppm $\pm$ 0.13 and 0.54 mg/m^3 $\pm$ 0.24 for NO_2 and PbClBr , respectively.



2. Particle Size Determination

The mean and geometric deviation of all count particle size determinations for PbClBr converted to mass median diameter (MMD) were $0.550 \mu \pm 1.57$ and $0.845 \mu \pm 1.75$ for Groups III and IV, respectively. Composite size versus distribution log-probability curves from the pooled count data are presented in Figures 33 and 34 for Groups III and IV, respectively.

3. Biological Measurements

3.1. Body Weight

Inspection of the growth curves (Figure 35) for these groups indicated a trend toward increasing body weight values in all groups.

Analysis of variance of regression for body weight (Table 4, Appendix B) revealed no significant difference in slopes among the groups.

3.2. Survival

No deaths occurred in Group I, Group III, or Group IV during the 104-week exposure period. Similarly, no deaths occurred in Group II during 87 weeks of exposure. Daily examination of the animals revealed no signs of toxicity or abnormal behavior attributable to the exposure atmospheres.

3.3. Pulmonary Function Tests

3.3.1. Mechanical Properties of the Lung and Respiratory System

3.3.1.1. Total Respiratory System Flow Resistance During Inspiration [Rrs(i)]

Analysis of variance of regression for Rrs(i) (Table 5, Appendix B) revealed non-parallelism among the groups. The third degree polynomial regression curves (Figure 36) revealed that Rrs(i) values for Groups III

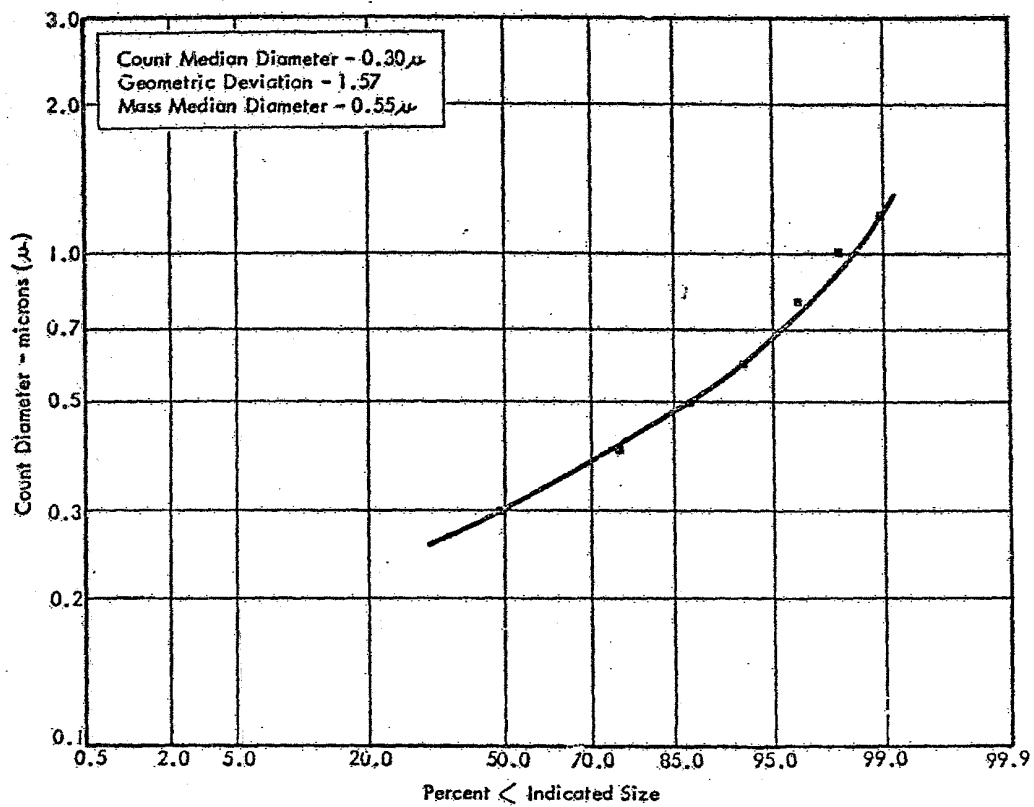


Figure 33 - Particle size distributions (count diameter) of $PbClBr$.

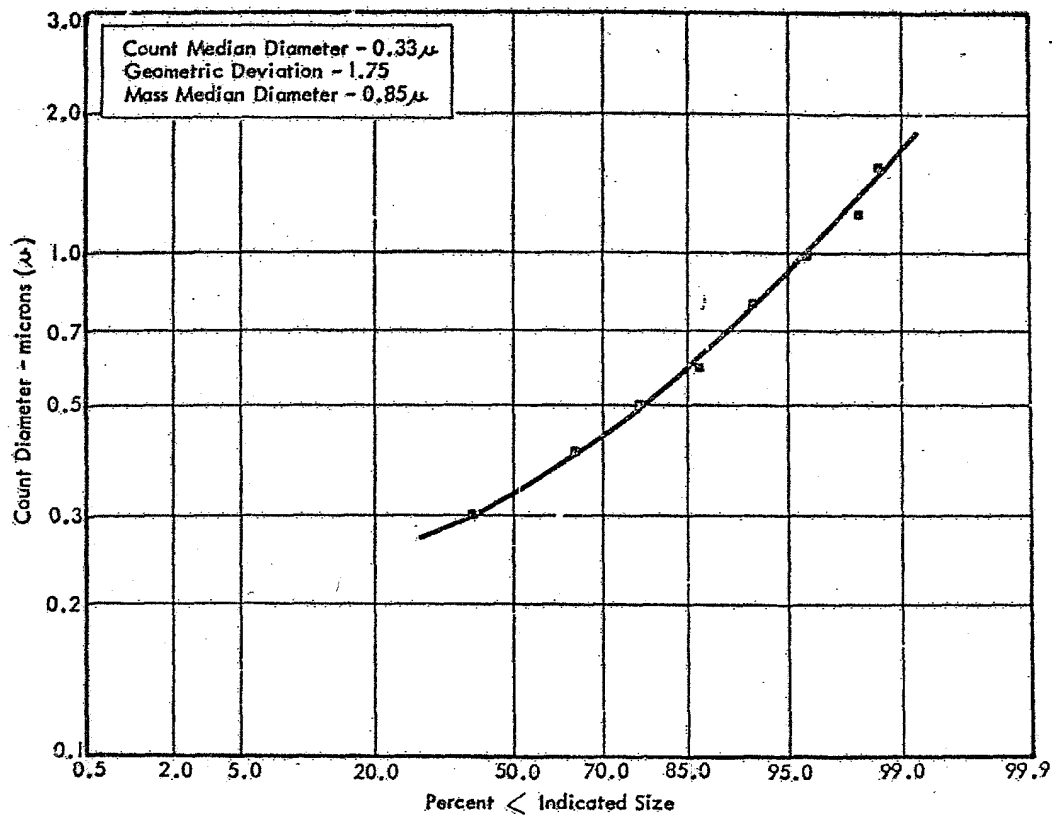


Figure 34 - Particle size distributions (count diameter) of PbClBr for the group exposed to the combination of PbClBr and NO₂.

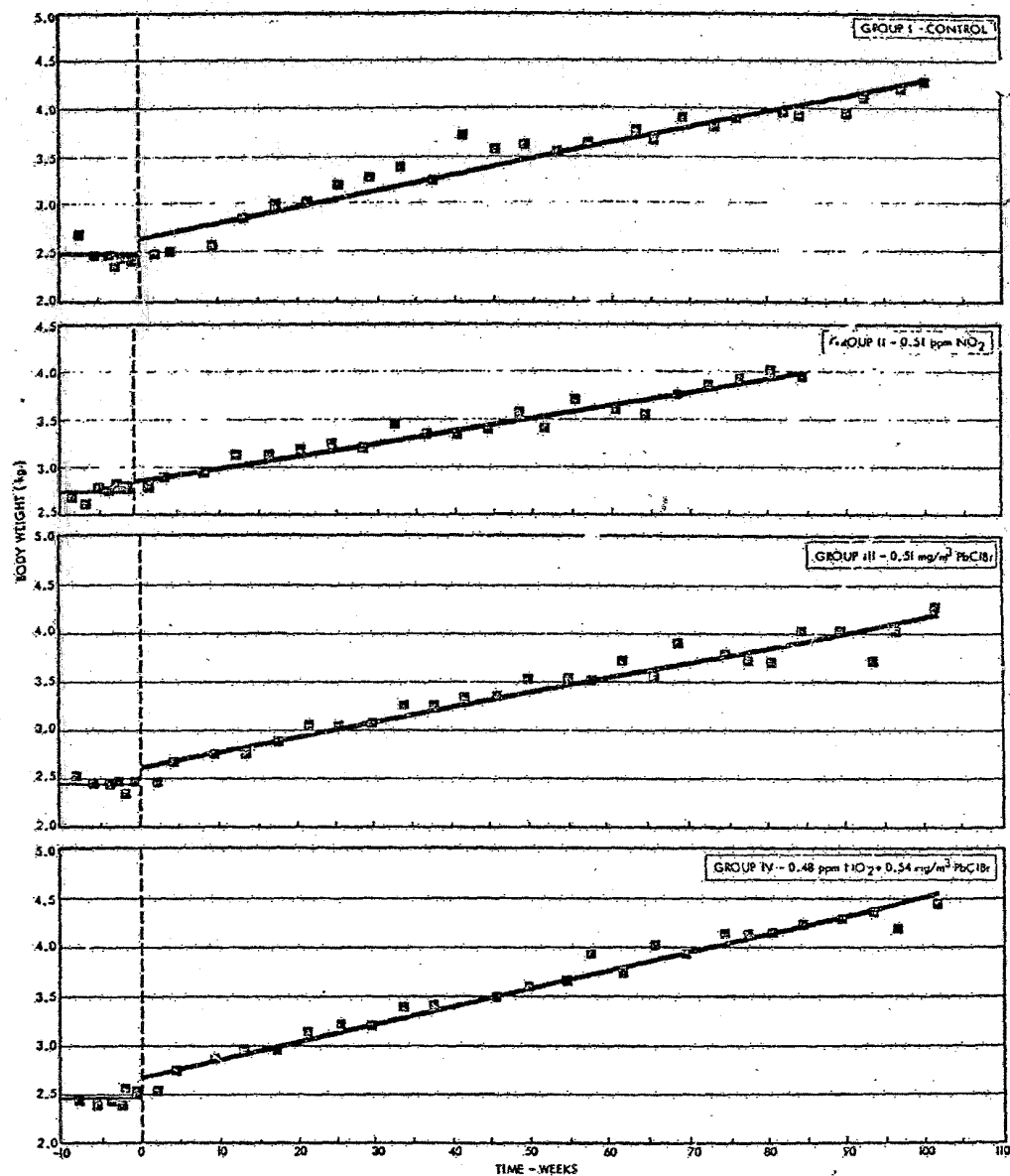


Figure 35 - First degree polynomial regression curves for body weight prior to and during exposure to nitrogen dioxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.

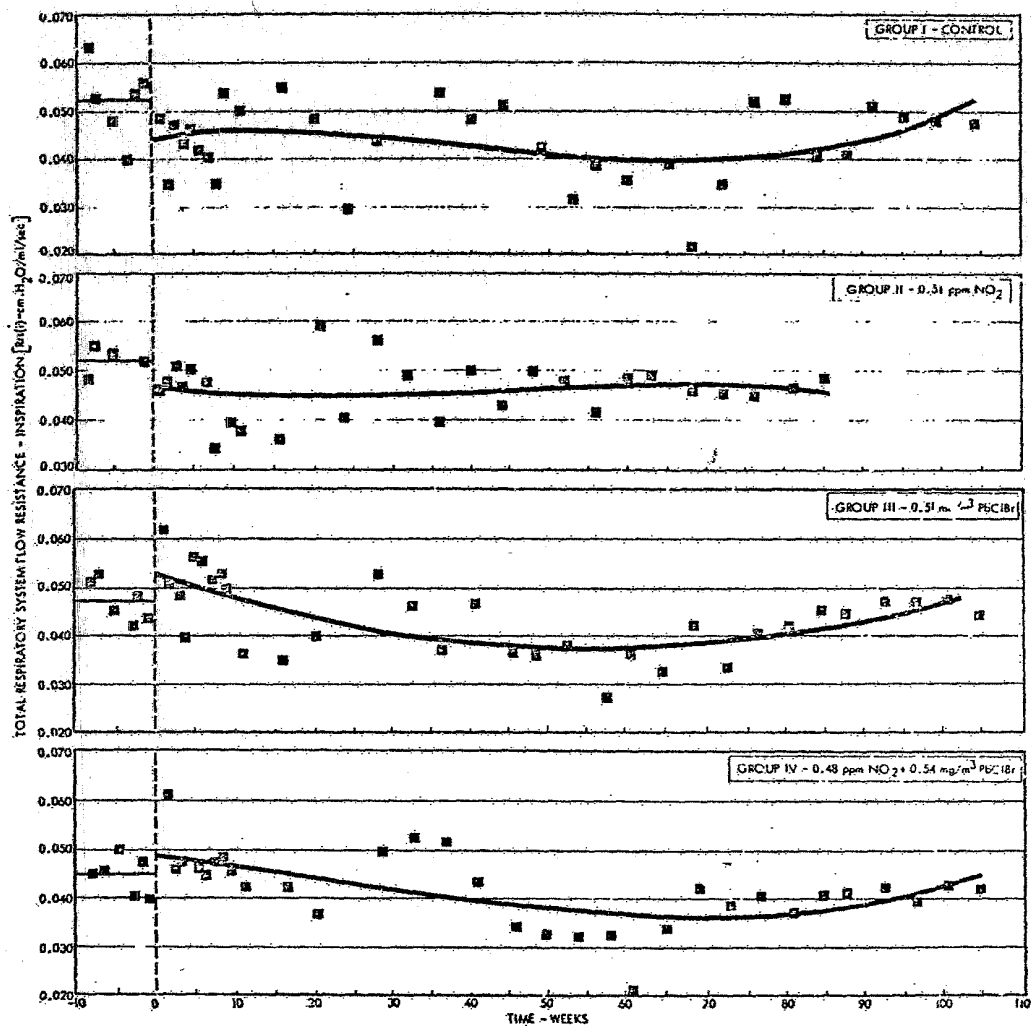


Figure 36 - Third degree polynomial regression curves for $R_{rs}(i)$ prior to and during exposure to nitrogen dioxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.



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and IV were slightly higher than values for Group I during the first nine weeks of exposure and that they thereafter were similar to Group I.

Separate t-tests of the pre-exposure adjusted means for the first nine weeks showed that both Groups III and IV were significantly higher than Group I during this period ($t = 4.33$, d.f. = 16 and $t = 3.92$, d.f. = 16, respectively).

3.3.1.2. Total Respiratory System Flow Resistance During Expiration [Rrs(e)]

Analysis of variance of regression for Rrs(e) (Table 6, Appendix B) indicated non-parallelism among the groups. The third degree polynomial regression curves (Figure 37) indicated a similar trend with time in Groups I, III, and IV, while Rrs(e) values for Group II remained at essentially the same level throughout the exposure period.

3.3.1.3. Tidal Volume (V_T)

Analysis of variance of regression for V_T (Table 7, Appendix B), revealed no significant differences in slopes among the groups. The third degree polynomial regression curves (Figure 38) indicated that all groups exhibited a similar upward trend with time, with Group II having slightly higher V_T values prior to exposure than the other groups.

3.3.1.4. Respiratory Rate (RR)

Analysis of variance of regression for RR (Table 8, Appendix B) indicated non-parallelism among the groups. The third degree polynomial regression curves (Figure 39) indicated that all groups except Group IV exhibited a slight decrease with time. RR for Group IV remained at essentially the same level throughout the exposure period,

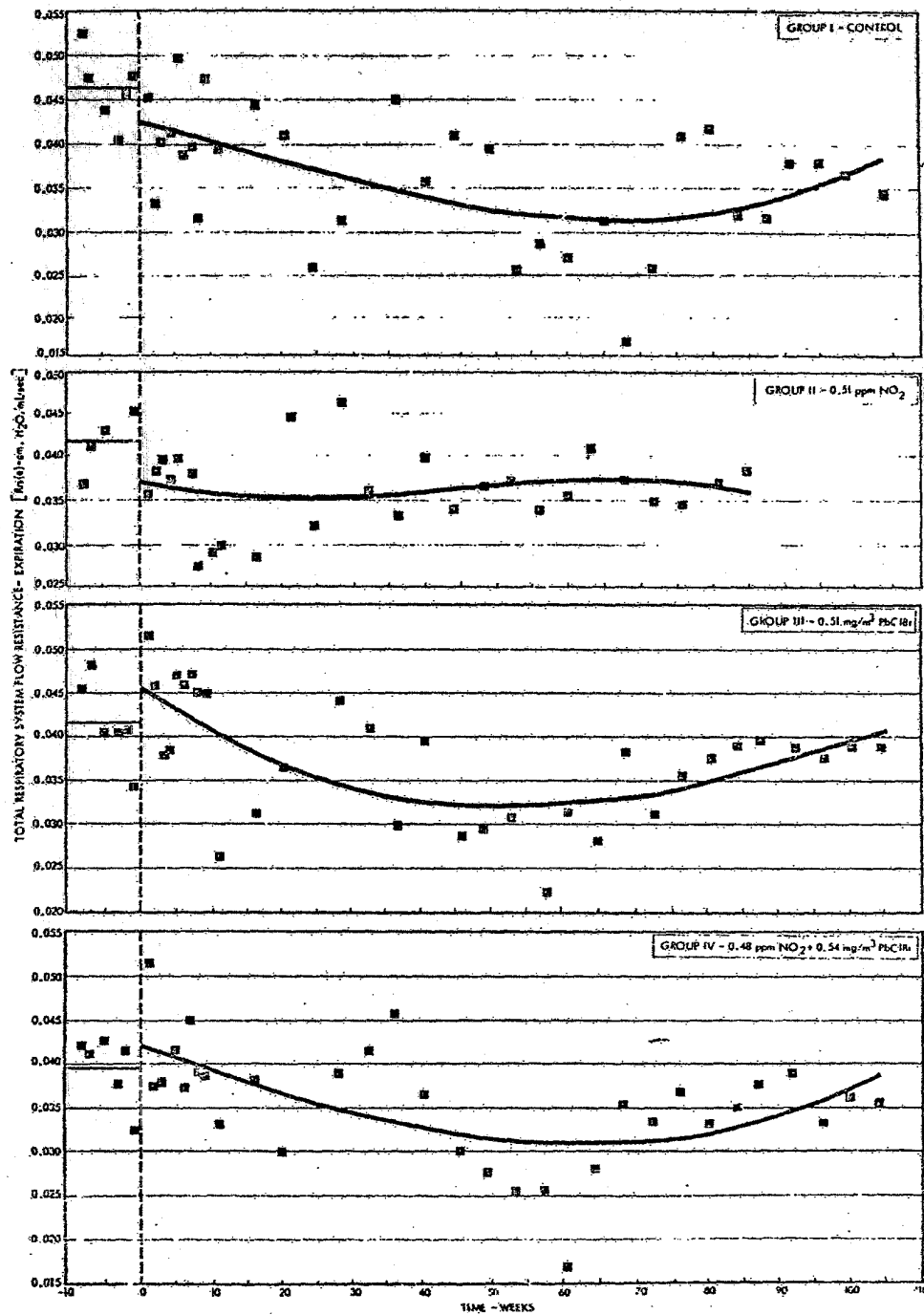


Figure 37 - Third degree polynomial regression curves for $R_{rs}(e)$ prior to and during exposure to nitrogen dioxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.

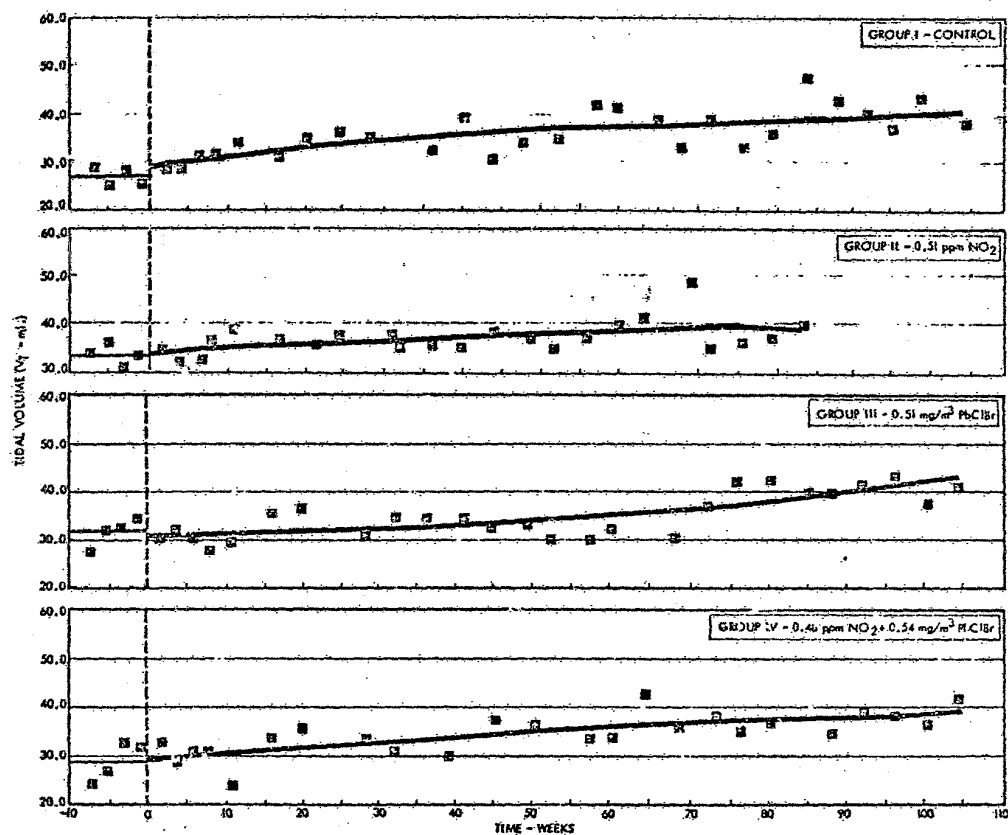


Figure 38 - Third degree polynomial regression curves for V_t prior to and during exposure to nitrogen dioxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.

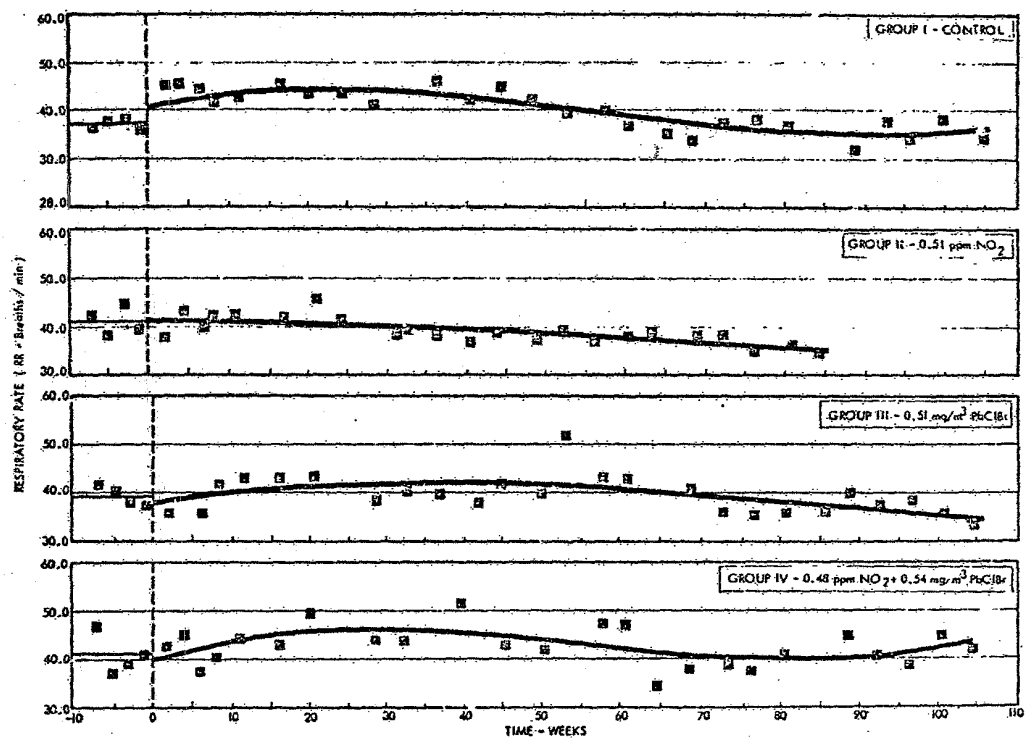


Figure 39 - Third degree polynomial regression curves for RR prior to and during exposure to nitrogen dioxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.



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3.3.1.5. Dynamic Compliance of the Lung [Cdyn(l)]

Analysis of variance of regression for Cdyn(l) (Table 9, Appendix B) revealed no significant differences in slopes among the groups. Figure 40 shows the third degree polynomial regression curves for the four groups which all increased with time. Although the pre-exposure adjusted means of the first year were significantly different between Groups I and III ($t = 2.69$, d.f. = 16), the fact that Group I showed a large increase at the start of exposure renders any interpretation difficult.

3.3.1.6. Pulmonary Flow Resistance (Rl)

Analysis of variance of regression for Rl (Table 10, Appendix B) indicated non-parallelism among the groups. The third degree polynomial regression curves (Figure 41) indicated that Groups III and IV increased slightly at the beginning of exposure and decreased thereafter, whereas Groups I and II remained nearly the same after an initial decrease. Separate t-tests of the pre-exposure adjusted means of the first nine weeks indicated that for this early interval the difference between Groups I and IV was not significant ($t < 1.64$, d.f. = 16), but Group III was significantly higher than Group I during this period ($t = 2.66$, d.f. = 16).

3.3.1.7. Work of Breathing During Inspiration per ml Tidal Volume [W(i)/ml V_T]

Analysis of variance of regression for W(i)/ml V_T (Table 11, Appendix B) revealed non-parallelism among the groups. The third degree polynomial regression curves (Figure 42) revealed only that Group II began the study slightly lower than the other groups and increased slightly to end at the level of the others. Values for Group III were lower than for Group I throughout the exposure period.

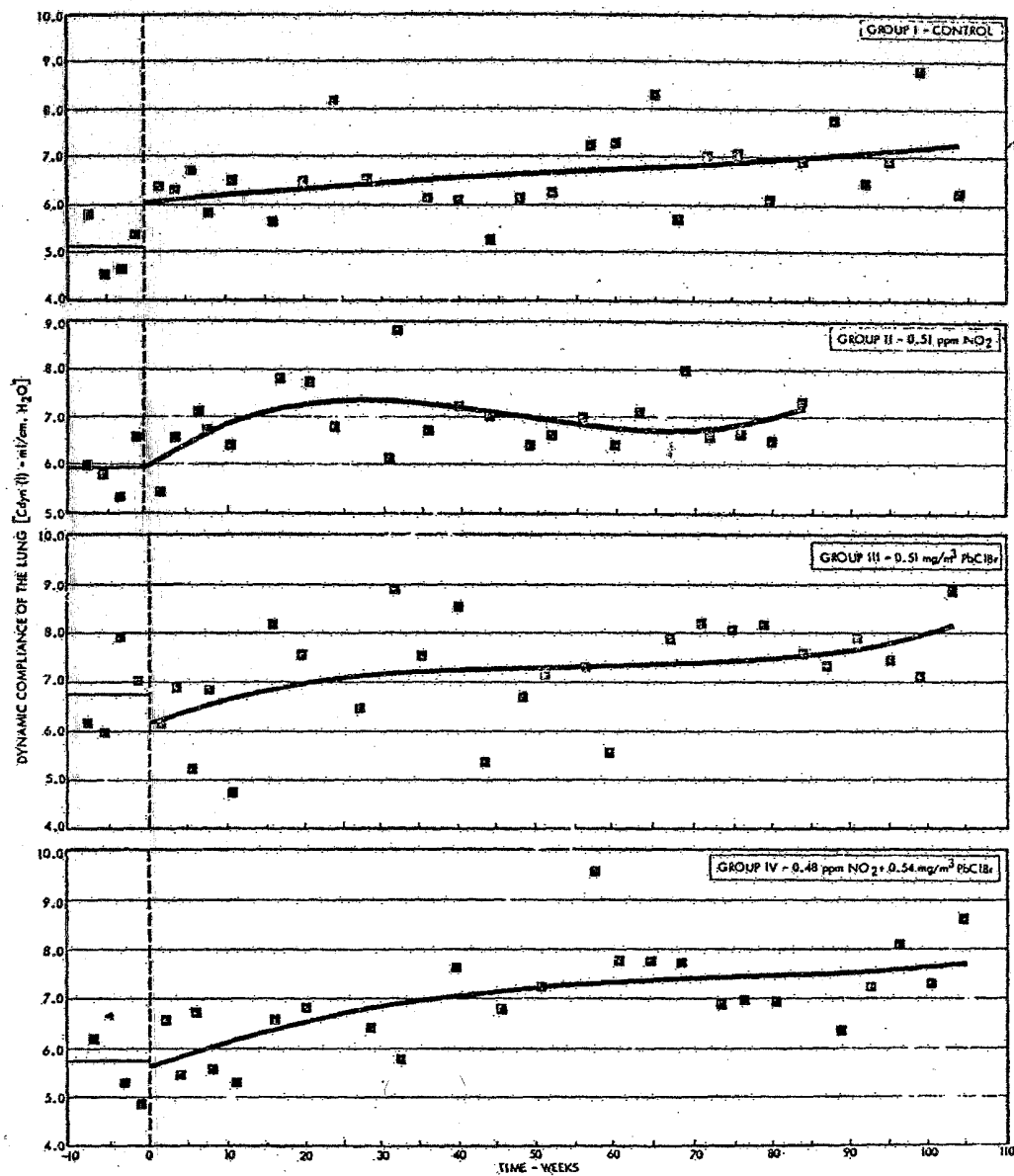


Figure 40 - Third degree polynomial regression curves for C_{dyn}(1) prior to and during exposure to nitrogen dioxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.

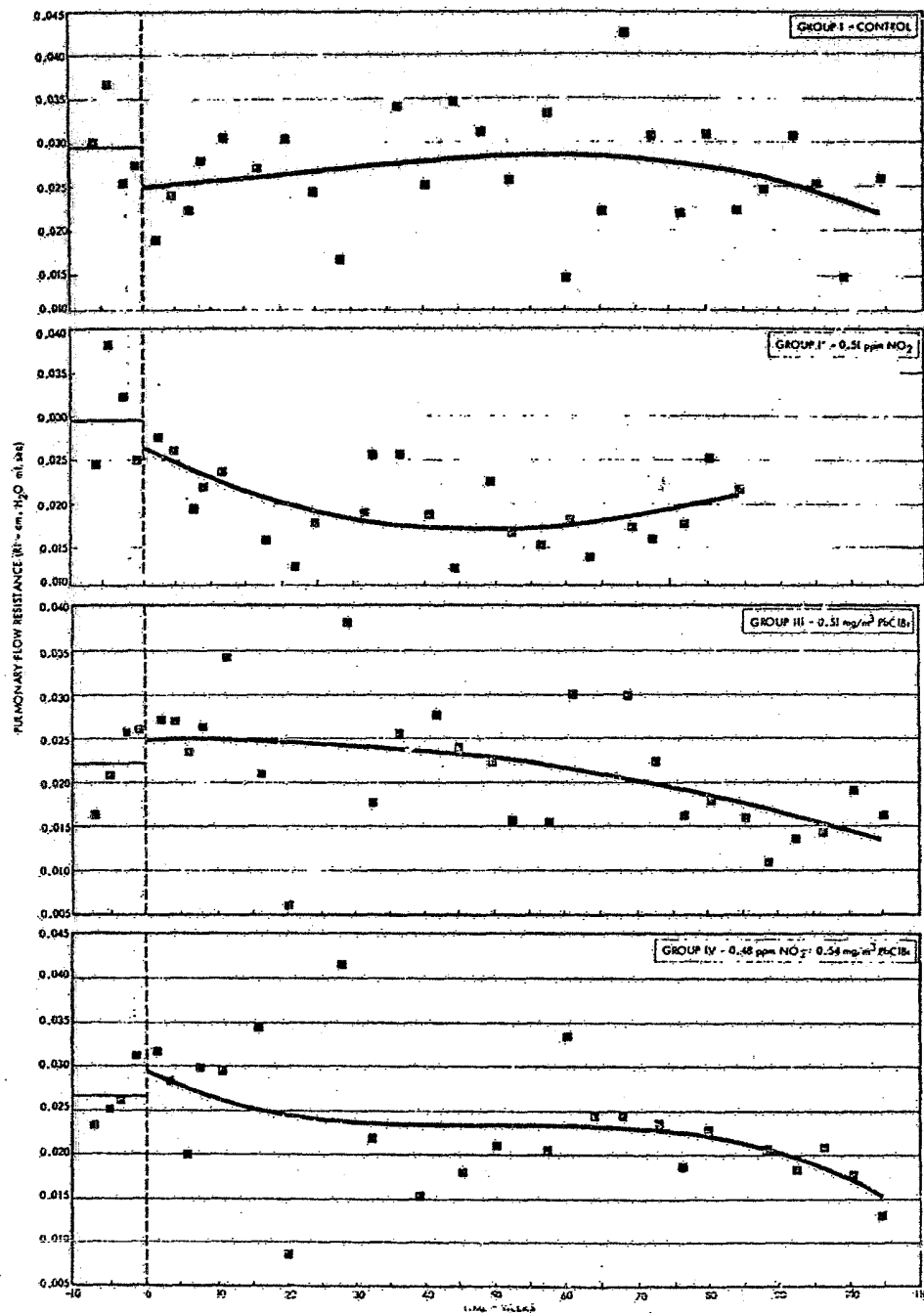


Figure 41 - Third degree polynomial regression curves for Rl prior to and during exposure to nitrogen dioxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.

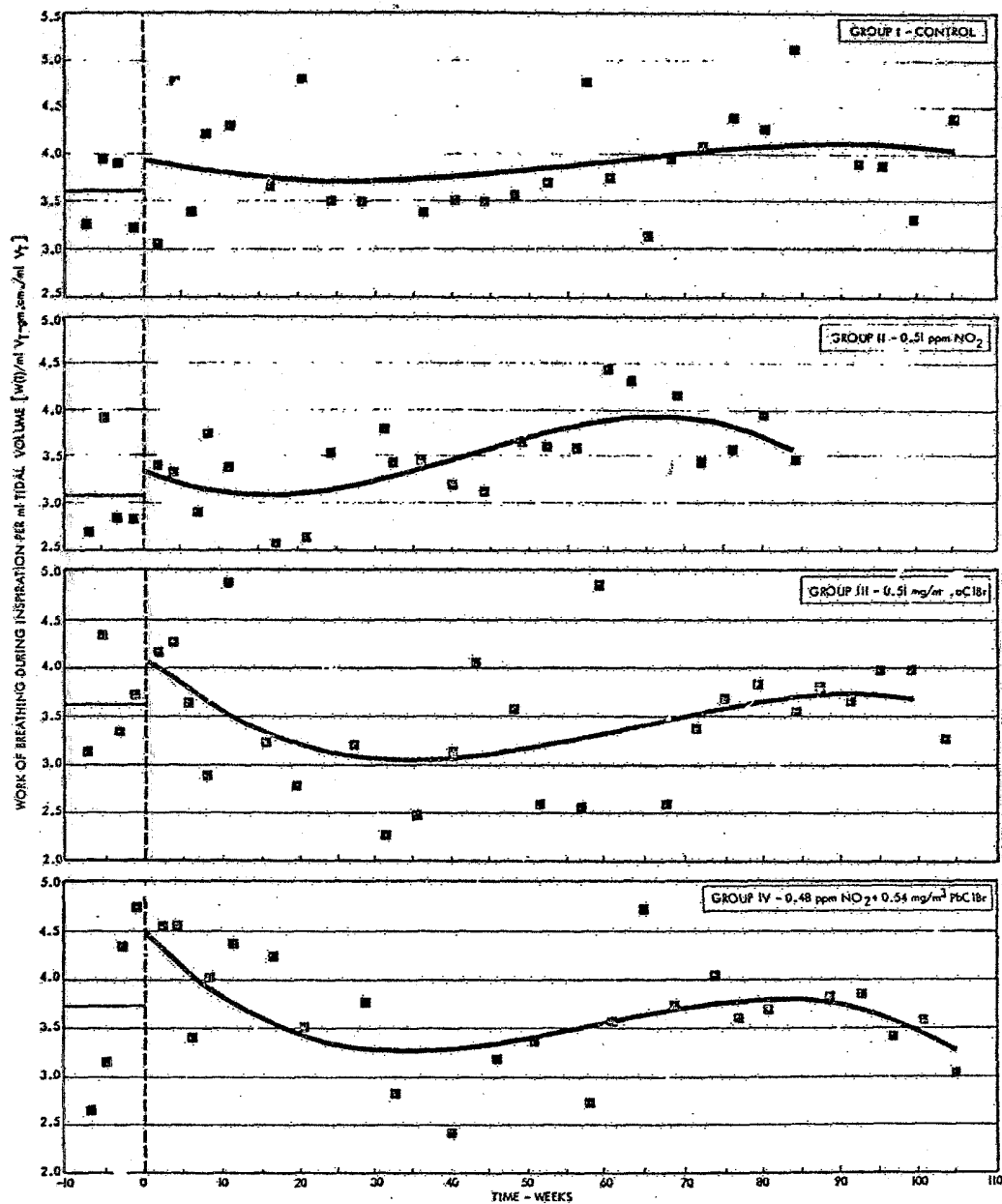


Figure 42 - Third degree polynomial regression curves for $W(i)/ml V_T$ prior to and during exposure to nitrogen dioxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.



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3.3.1.8. Work of Breathing During Expiration per ml Tidal Volume $[W(e)/ml V_T]$

Analysis of variance of regression for $W(e)/ml V_T$ (Table 12, Appendix B) indicated no significant slope differences among the groups. Figure 43 shows the third degree polynomial regression curves for the groups.

3.3.2. Diffusing Capacity of the Lung for Carbon Monoxide (DL_{CO})

Analysis of variance of regression for DL_{CO} (Table 13, Appendix B) revealed no significant differences in slopes among the groups. Figure 44 shows the third degree polynomial regression curves for the groups which all increased with time.

3.3.3. Distribution of Inspired Air, Nitrogen Washout

3.3.3.1. Number of Breaths from 80% to 1% Nitrogen $[N(1\% N_2)]$

Analysis of variance of regression for $N(1\% N_2)$ (Table 14, Appendix B) indicated no significant slope differences among the groups. The third degree polynomial regression curves (Figure 45), however, indicated that Groups III and IV both exhibited a rapid rise during exposure, whereas, Groups I and II remained at their pre-exposure levels. Since Groups III and IV remained relatively level after the initial rise, their overall pre-exposure adjusted exposure means were compared by t-tests to Group I. Both Groups III and IV differed significantly from Group I ($t = 4.55$, d.f. = 16; $t = 4.07$, d.f. = 16, respectively).

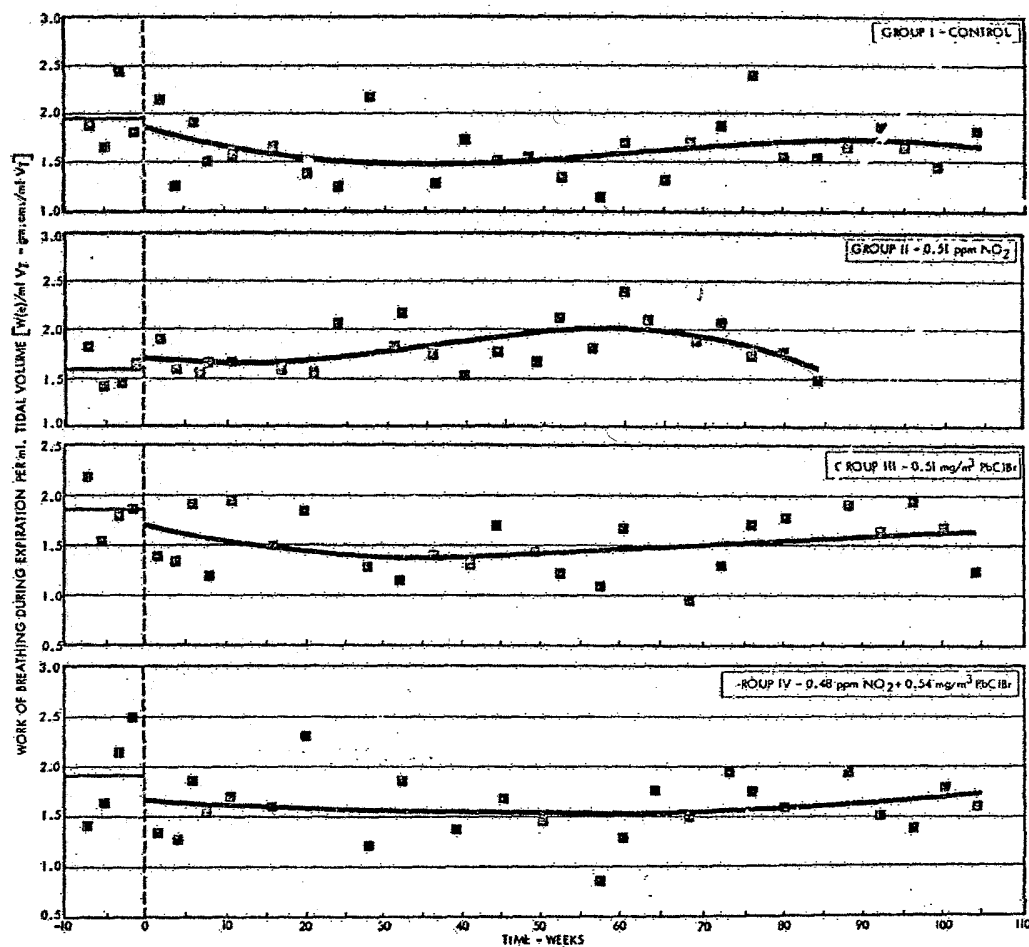


Figure 43 - Third degree polynomial regression curves for $W(e)/ml V_T$ prior to and during exposure to nitrogen dioxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.

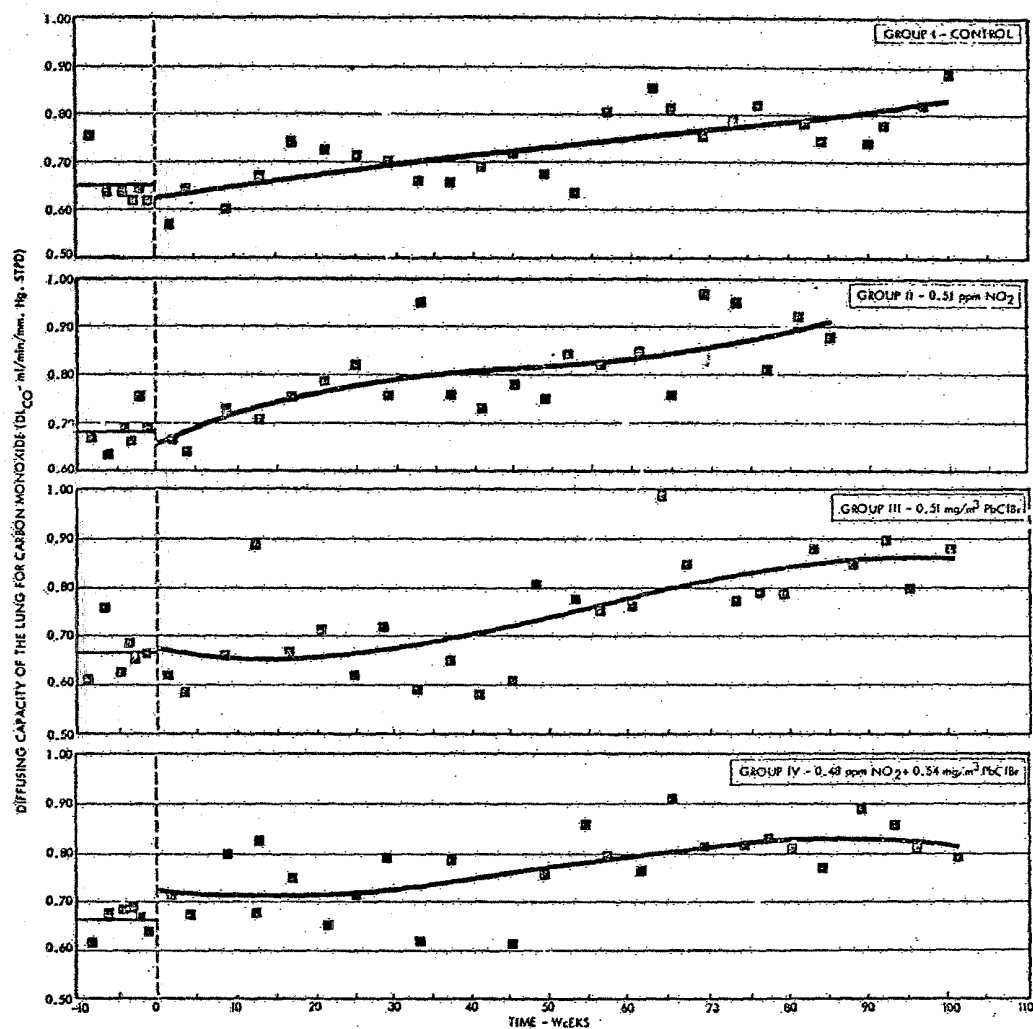


Figure 44 - Third degree polynomial regression curves for DLCO prior to and during exposure to nitrogen dioxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.

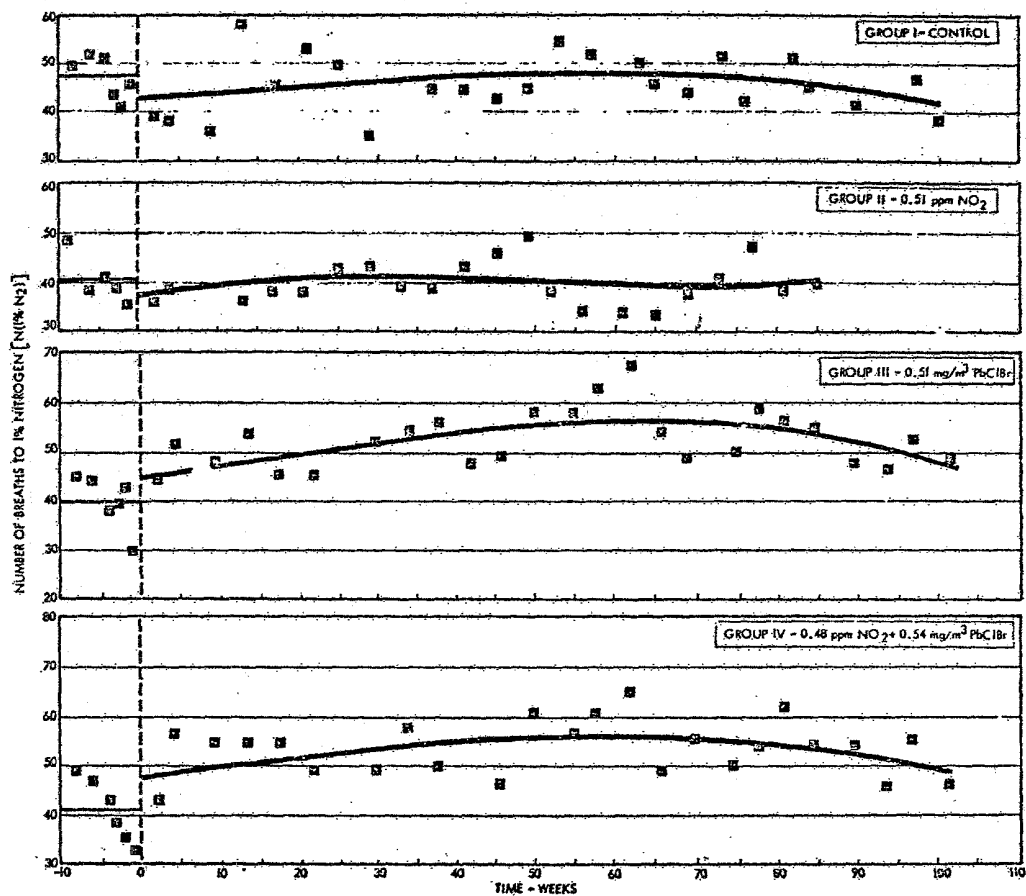


Figure 45 - Third degree polynomial regression curves for N(1% N₂) prior to and during exposure to nitrogen dioxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.



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3.3.3.2. Respiratory Rate Measured During Pure Oxygen Breathing (RR')

Analysis of variance of regression for RR' (Table 15, Appendix B) showed significant slope differences among the groups. The third degree regression curves (Figure 46) indicated that RR' for Groups I and II was similar prior to exposure and through Week 50 of the exposure period. From Week 50 to the end of the exposure period, Group I exhibited lower RR' values than Group II, although Group II was decreasing consistently through the first eight intervals prior to termination at Week 84. A t-test of the pre-exposure adjusted means for the time segment Week 53 to 84 indicated a barely significant difference ($t = 2.15$, d.f. = 16). A similar test of the overall exposure means of these two groups, however, was not significant ($t = 1.90$, d.f. = 16).

Further inspection of Figure 46 indicated that Group III, when compared to Group I, had higher RR' values starting at Week 45. A CUSUM plot of the time-paired differences between Group I and Group III (Figure 47) indicated that a change in the differences of the mean RR' levels occurred at Week 45 of the exposure period. RR' data for Groups I and III were therefore separated into the following time segments, 1) the pre-exposure control period, 2) from the beginning of exposure to Week 45, and 3) exposure period from Week 49 to the end. A t-test of these pre-exposure adjusted means for the last time segment indicated a significant difference between the groups ($t = 2.94$, d.f. = 16). The earlier time segment was not significantly different ($t = 1.65$, d.f. = 16). A similar test of the overall exposure means of these two groups, however, was also significant ($t = 2.61$, d.f. = 16).

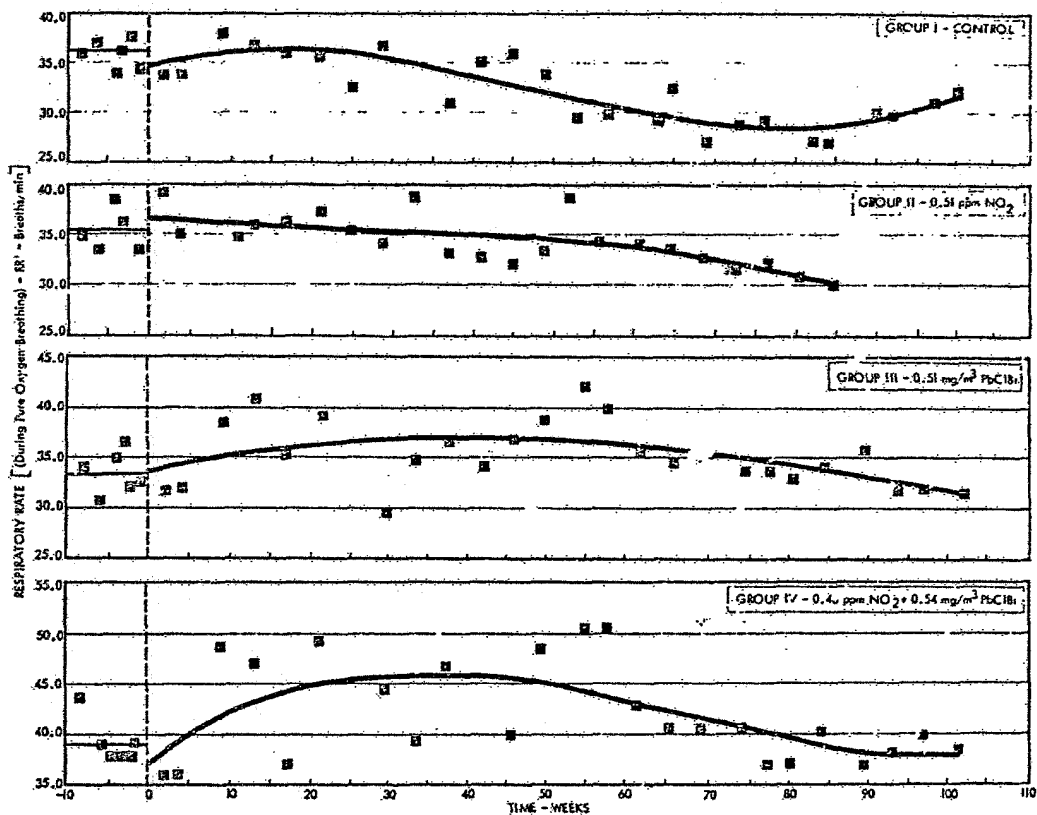


Figure 46 - Third degree polynomial regression curves for RR' prior to and during exposure to nitrogen dioxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.

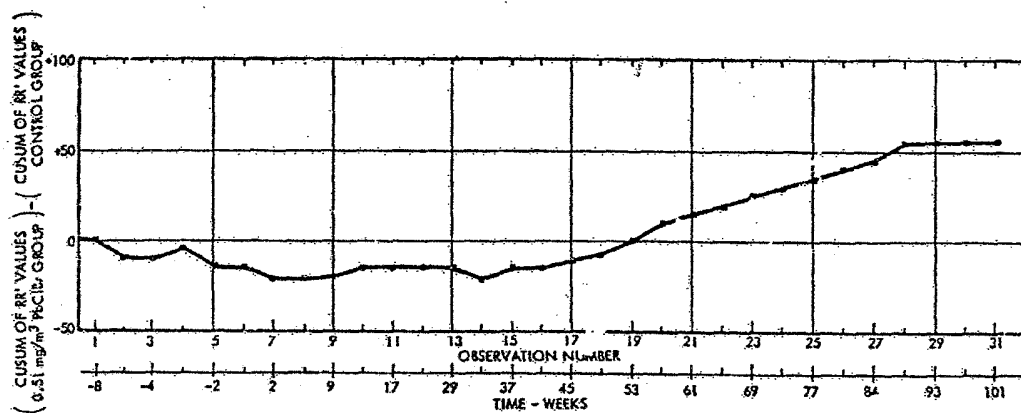


Figure 47 - The time-paired differences between the cumulative sums of RR' between Groups I and III (control and 0.51 mg/m³ PbCl₂).



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A t-test of the pre-exposure adjusted overall exposure means between Groups I and IV indicated that Group IV was significantly higher ($t = 3.69$, d.f. = 16) throughout the exposure period. Similar tests comparing Groups II and IV and Groups III and IV revealed that Group IV was significantly higher ($t = 2.22$, d.f. = 16) than Group II, but was comparable to Group III ($t = < 1.64$, d.f. = 16).

3.3.3.3. Cumulative Tidal Volume from 80% to 1% Nitrogen [$CV_T(1\% N_2)$]

Analysis of variance of regression for $CV_T(1\% N_2)$ (Table 16, Appendix B) indicated no significant slope differences among the groups. Figure 48 shows the third degree polynomial regression curves for the four groups which increased with time. Values for Group III were slightly higher overall than Group I throughout the exposure period. A t-test of the pre-exposure adjusted overall exposure means comparing Groups I and III indicated that Group III was significantly higher ($t = 2.24$, d.f. = 13.7) throughout the exposure period.

3.3.3.4. Tidal Volume Measured During Pure Oxygen Breathing (V_T')

Analysis of variance of regression for V_T' (Table 17, Appendix B) revealed no significant slope differences among the groups. Figure 49 shows the third degree polynomial regression curves for the four groups.

3.4. Hematology

The group means and analysis of variances of the various hematological variables measured are presented in Tables 18, 19, 20, and 21, Appendix B. No consistent trends were noted in any of these variables which remained within normal limits throughout. Random statistically significant differences were seen, but were not consistently related to the exposure conditions.

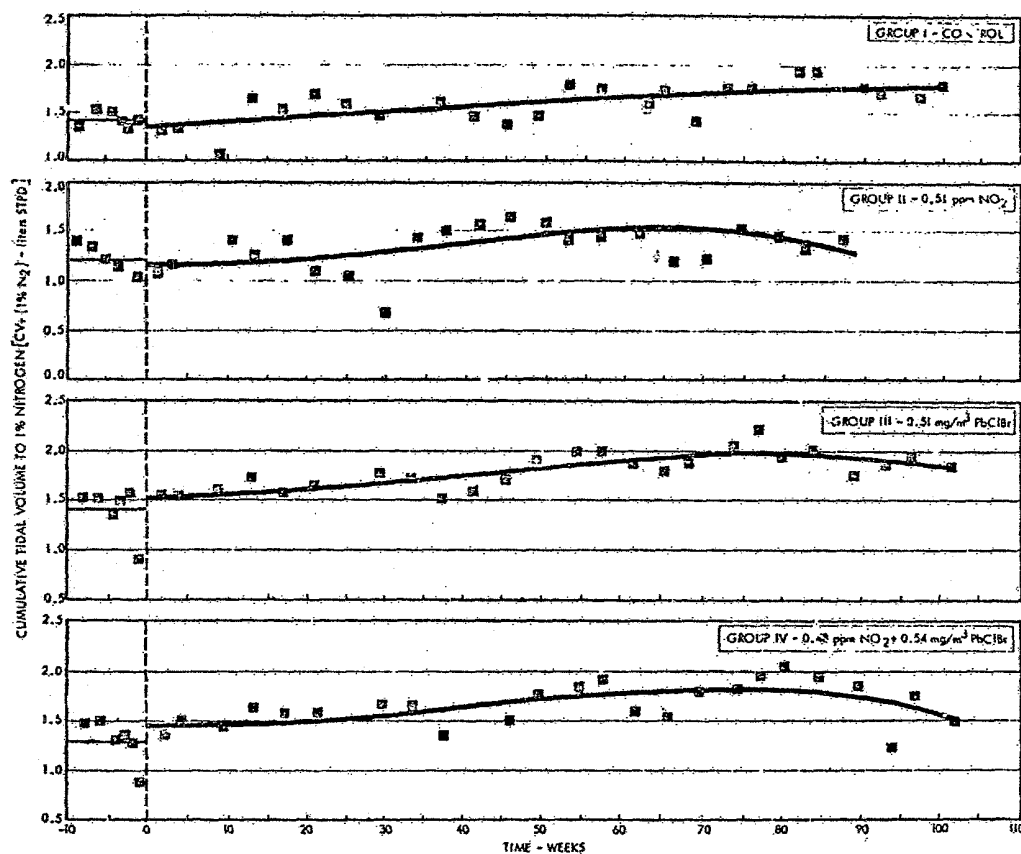


Figure 48 - Third degree polynomial regression curves for CV_T(1% N₂) prior to and during exposure to nitrogen dioxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.

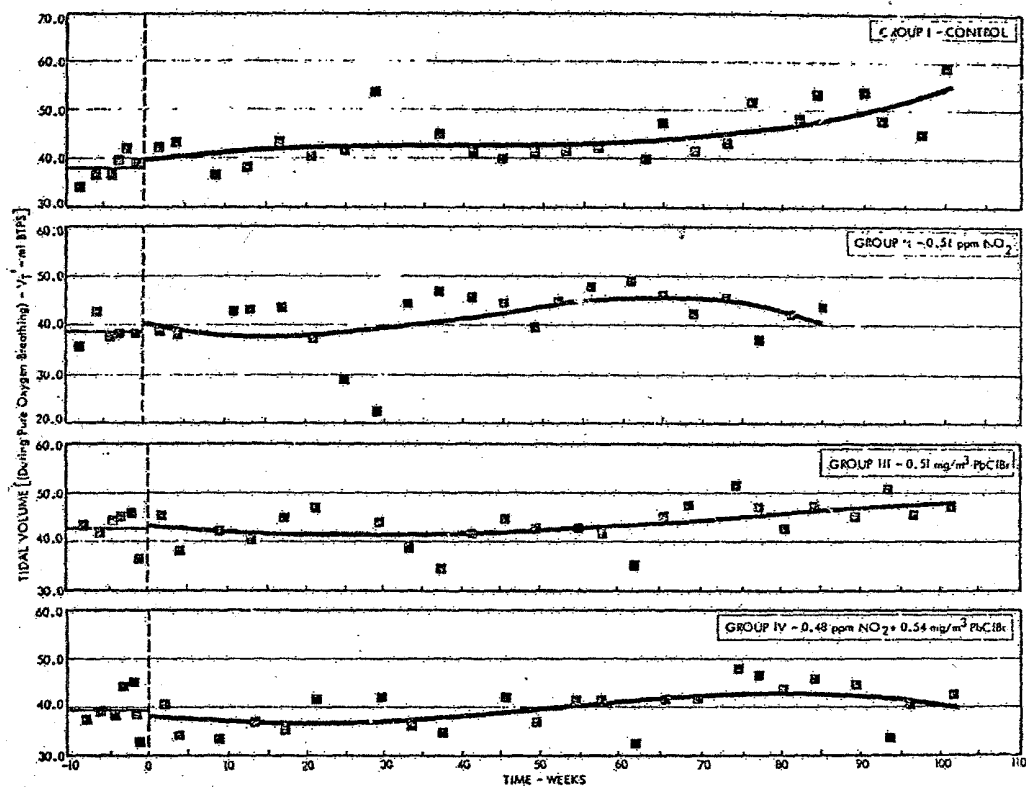


Figure 49 - Third degree polynomial regression curves for V_T prior to and during exposure to nitrogen dioxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.



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3.5. Clinical Biochemistry

The group means, standard errors, and the results of the analysis of variance of the various clinical biochemical variables measured are presented in Tables 22 through 35, Appendix B. Scattered statistically significant differences were noted; however, no trends were seen in any of the variables. Throughout the study, the group mean values fluctuated within the normal ranges of these variables.

3.6. Arterial Blood Gas and pH

The group means and standard errors for the blood gas variables are presented in Table 36, Appendix B. Examination of these data did not reveal any consistent trend with time. No apparent exposure-related changes were seen in any of these variables.

3.7. Terminal Body Weight, Organ Weight, and Organ Weight as a Percentage of Body Weight

The data of the terminal body weight, organ weight, and organ/body weight ratios for Groups I, II, III, and IV are presented in Tables 37 and 38, Appendix B, for males and females, respectively. Single classification analysis of variance revealed that the brain weight for the males in Group IV was significantly lower than the males in Group I and that the adrenal weight for the males in Group II was significantly lower than for Group IV males. Adrenal weight and adrenal weight/body weight ratios for the females in Group III were significantly higher than for Group II females. Adrenal weight/body weight ratio for Group III females was also significantly higher than Group IV females. The liver weight/body weight ratio for the females in Group II was significantly lower than for Group IV females.



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3.8. Histopathology Summary

A detailed listing of the microscopic alterations seen in the lungs, tracheas, livers, kidneys, peribronchial lymph nodes, and hearts from the animals in the control and exposure groups are found in Table 39, Appendix B. Microscopic alterations related to the exposure to PbClBr were seen in the kidneys of the animals exposed to 0.6 mg/m^3 of PbClBr alone and of those exposed to the combination of 0.6 mg/m^3 of PbClBr and 0.5 ppm NO_2 . These microscopic alterations were characterized by varying degrees of degeneration in the proximal convoluted tubules. The epithelial cells of the proximal convoluted tubules were slightly to moderately vacuolated, and there were varying degrees of loss of the brush border and of nuclear vesiculation in these cells. Acid fast intranuclear inclusion bodies were seen in the epithelial cells of the proximal convoluted tubules in seven of the nine animals exposed to 0.6 mg/m^3 PbClBr alone and in nine of the nine animals exposed to the combination of 0.6 mg/m^3 PbClBr and 0.5 ppm NO_2 .

No exposure-related microscopic alterations were seen in the lungs, livers, peribronchial lymph nodes, tracheas, or hearts from the animals exposed to NO_2 alone, to PbClBr alone, or to the combination of NO_2 and PbClBr . A moderate amount of brownish granular birefringent pigment was seen in the macrophages lining the sinusoids of the livers from the animals exposed to 0.5 ppm NO_2 . A similar type of pigment was seen in two of the nine animals in the control group and two of nine animals each in the groups exposed to 0.6 mg/m^3 of PbClBr alone and the group exposed to the combination of 0.6 mg/m^3 of PbClBr and 0.5 ppm NO_2 . The etiology of this pigment was not demonstrable in the sections examined.



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3.9. Summary

The inhalation exposure of male and female cynomolgus monkeys to 0.51 ppm NO_2 , 0.51 mg/m^3 of lead chlorobromide (PbClBr), and the combination of 0.48 ppm NO_2 plus 0.54 mg/m^3 PbClBr resulted in a deterioration in the distribution of ventilation in the animals in the two groups containing PbClBr .

The number of breaths to 1% nitrogen measured during pure oxygen breathing was significantly elevated in the animals in both groups exposed to PbClBr . No increase in the number of breaths to 1% nitrogen was detected in the animals exposed to 0.51 ppm NO_2 alone.

Respiratory rate measured during pure oxygen breathing was significantly elevated in the group exposed to NO_2 alone during the latter half of the study only, but was significantly elevated throughout the exposure period in the groups exposed to PbClBr alone and to the combination of PbClBr and NO_2 .

Microscopic alterations related to the exposure to PbClBr were found in the kidneys of the animals in these two groups. These histopathological changes were characterized by varying degrees of degeneration of the proximal convoluted tubules. The epithelial cells of the proximal convoluted tubules were slightly to moderately vacuolated, possessed irregular luminal borders, and in several areas, had lost their brush border. The nuclei of these epithelial cells were vesiculated and many contained acid fast, intranuclear inclusion bodies.



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Body weight measurements made on both the control and exposed animals throughout the exposure period indicated that the animals in all groups increased in body weights. Analysis of these data did not reveal any significant differences in the rate of growth between the control and exposed animals. Terminal body weights, organ weights, and organ/body weight ratios for the control and exposed animals were compared. No meaningful differences were detected in these variables between the control and exposed groups.

Hematological, clinical biochemical, and arterial blood gas measurements were made on both the control and exposed animals pre-exposure and periodically throughout the exposure period. No trends were detected in any of these variables in the exposed animals. No meaningful differences were detected between the control and exposed animals.



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Appendix B - Data compilations and summary of statistical analysis for

Statistical Grouping B, comprised of the following:

Group I - Control, Group II - 0.51 ppm NO₂, Group III -

0.51 mg/m³ PbClBr, and Group IV - 0.48 ppm NO₂ +

0.54 mg/m³ PbClBr.

Table 1 - Monthly means and the grand mean for the analytical concentrations of nitrogen dioxide for Group II.

<u>Date</u>	<u>n</u>	<u>$\bar{x}$</u> ppm	<u>S.D.</u>
1/12/69- 1/31/69	20	0.4875	0.0477
2/ 1/69- 2/28/69	28	0.4843	0.0813
3/ 1/69- 3/31/69	31	0.4997	0.0561
4/ 1/69- 4/30/69	30	0.5343	0.0710
5/ 1/69- 5/31/69	31	0.5277	0.0553
6/ 1/69- 6/30/69	30	0.4790	0.0911
7/ 1/69- 7/31/69	31	0.4255	0.0721
8/ 1/69- 8/31/69	31	0.4813	0.0471
9/ 1/69- 9/30/69	30	0.5090	0.0575
10/ 1/69-10/31/69	31	0.4842	0.0828
11/ 1/69-11/30/69	30	0.4787	0.0734
12/ 1/69-12/31/69	31	0.5023	0.0794
1/ 1/70- 1/31/70	31	0.5264	0.0670
2/ 1/70- 2/28/70	28	0.5093	0.0468
3/ 1/70- 3/31/70	31	0.5077	0.0439
4/ 1/70- 4/30/70	30	0.5147	0.0324
5/ 1/70- 5/31/70	31	0.5365	0.0336
6/ 1/70- 6/30/70	30	0.5113	0.0251
7/ 1/70- 7/31/70	31	0.5339	0.0434
8/ 1/70- 8/31/70	31	0.5116	0.0288
9/ 1/70- 9/11/70	11	0.5073	0.0210

N = 21

$\bar{X}$ = 0.51

S.D. = 0.06

Table 2 - Monthly means and the grand mean for the analytical concentrations of lead chlorobromide for Group III.

<u>Date</u>	<u>n</u>	<u>$\bar{x}$</u> <u>mg/m³</u>	<u>S.D.</u>
5/11/68- 5/31/68	20	0.8570	1.0552
6/ 1/68- 6/30/68	30	0.4743	0.6379
7/ 1/68- 7/31/68	31	0.4565	0.3048
8/ 1/68- 8/31/68	31	0.6022	0.1088
9/ 1/68- 9/30/68	30	0.5773	0.1526
10/ 1/68-10/31/68	31	0.5074	0.1497
11/ 1/68-11/30/68	30	0.4286	0.1944
12/ 1/68-12/31/68	31	0.4638	0.1819
1/ 1/69- 1/31/69	31	0.4752	0.1339
2/ 1/69- 2/28/69	28	0.6154	0.7173
3/ 1/69- 3/31/69	31	0.5677	0.1515
4/ 1/69- 4/30/69	30	0.5147	0.2131
5/ 1/69- 5/31/69	31	0.7770	0.1710
6/ 1/69- 6/30/69	30	0.5503	0.1740
7/ 1/69- 7/31/69	31	0.5597	0.2216
8/ 1/69- 8/31/69	31	0.5010	0.1545
9/ 1/69- 9/30/69	30	0.4737	0.2049
10/ 1/69-10/31/69	31	0.5352	0.2722
11/ 1/69-11/31/69	30	0.4930	0.0363
12/ 1/69-12/31/69	31	0.3871	0.1065
1/ 1/70- 1/31/70	31	0.4052	0.2503
2/ 1/70- 2/28/70	28	0.5100	0.3669
3/ 1/70- 3/31/70	31	0.5561	0.2526
4/ 1/70- 4/30/70	30	0.3070	0.5232
5/ 1/70- 5/ 5/70	5	0.1080	0.0295

N = 25

$\bar{X}$ = 0.51

S.D. = 0.27

Table 3 - Monthly means and the grand mean for the analytical concentrations of nitrogen dioxide and lead chlorobromide for experimental Group IV

Date	n	PbClBr		NO ₂	
		$\bar{x}$ mg/m ³	S.D.	$\bar{x}$ ppm	S.D.
5/11/68- 5/30/68	21	0.6938	0.4009	0.4590	0.1525
6/ 1/68- 6/30/68	30	0.5313	0.2659	0.5293	0.0818
7/ 1/68- 7/31/68	31	0.4229	0.2202	0.4538	0.1253
8/ 1/68- 8/31/68	29	0.6069	0.1938	0.4386	0.1197
9/ 1/68- 9/30/68	28	0.7018	0.2171	0.3900	0.1651
10/ 1/68-10/31/68	31	0.6332	0.2762	0.5052	0.1337
11/ 1/68-11/30/68	30	0.5513	0.2039	0.5007	0.1230
12/ 1/68-12/31/68	31	0.5655	0.1176	0.4726	0.0624
1/ 1/69- 1/31/69	31	0.4755	0.1776	0.4890	0.0638
2/ 1/69- 2/28/69	28	0.6718	0.6879	0.4711	0.0686
3/ 1/69- 3/31/69	31	0.5558	0.1991	0.4606	0.0657
4/ 1/69- 4/30/69	30	0.6893	0.2610	0.4826	0.0579
5/ 1/69- 5/31/69	31	0.6881	0.1563	0.4771	0.7721
6/ 1/69- 6/30/69	30	0.6783	0.1021	0.4770	0.3911
7/ 1/69- 7/31/69	31	0.5455	0.2489	0.5132	0.0768
8/ 1/69- 8/31/69	31	0.5739	0.1936	0.5206	0.0479
9/ 1/69- 9/30/69	30	0.5007	0.2448	0.4850	0.0730
10/ 1/69-10/31/69	31	0.4135	0.2207	0.4690	0.0927
11/ 1/69-11/30/69	30	0.4223	0.1588	0.4597	0.0653
12/ 1/69-12/31/69	31	0.4326	0.1230	0.4619	0.0769
1/ 1/70- 1/31/70	31	0.5581	0.2428	0.5187	0.0726
2/ 1/70- 2/28/70	28	0.4925	0.2157	0.5182	0.0502
3/ 1/70- 3/31/70	31	0.7639	0.6776	0.5100	0.0486
4/ 3/70- 4/30/70	30	0.2280	0.1403	0.5203	0.0335
5/ 1/70- 5/ 5/70	5	0.1760	0.0279	0.4980	0.1743
		N = 25		N = 25	
		$\bar{X}$ = 0.54		$\bar{X}$ = 0.49	
		S.D. = 0.24		S.D. = 0.13	

Table 4 - Summary of statistical analyses of body weight data for Statistical Grouping B, comprised of the following: Group I - Control, Group II - 0.51 ppm NO₂, Group III - 0.51 mg/m³ PbClBr, and Group IV - 0.48 ppm NO₂ + 0.54 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	2.023	6.744 x 10 ⁻¹	0.59	-
Error Deviation	913	1.044 x 10 ³	1.143	-	-

FIRST DEGREE POLYNOMIAL REGRESSION COEFFICIENTS					
GROUPS	REGRESSION COEFFICIENTS		S.E.	Sv.x	r
	A	B			
I	2.63 ± 0.052	1.64 x 10 ⁻² ± 8.93 x 10 ⁻⁴		0.14	0.96
II	2.85 ± 0.032	1.34 x 10 ⁻² ± 6.61 x 10 ⁻⁴		0.08	0.97
III	2.61 ± 0.046	1.53 x 10 ⁻² ± 8.02 x 10 ⁻⁴		0.13	0.97
IV	2.67 ± 0.039	1.80 x 10 ⁻² ± 6.64 x 10 ⁻⁴		0.11	0.98

Table 5 - Summary of statistical analyses of total respiratory system flow resistance during inspiration data for Statistical Grouping B, comprised of the following: Group I - Control, Group II - 0.51 ppm NO₂, Group III - 0.51 mg/m³ PbClBr, and Group IV - 0.48 ppm NO₂ + 0.54 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	1.407 x 10 ⁻³	4.691 x 10 ⁻⁴	3.90	Yes
Error Deviation	1113	1.337 x 10 ⁻¹	1.201 x 10 ⁻⁴	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.					n	r
	A	B	C	D	Sy.X		
I	0.044 ± 0.0033	2.12 x 10 ⁻⁴ ± 3.81 x 10 ⁻⁴	-9.72 x 10 ⁻⁶ ± 9.30 x 10 ⁻⁶	8.10 x 10 ⁻⁸ ± 6.10 x 10 ⁻⁸	0.008	39	0.37
II	0.047 ± 0.0029	-2.18 x 10 ⁻⁴ ± 3.85 x 10 ⁻⁴	7.00 x 10 ⁻⁶ ± 1.15 x 10 ⁻⁵	-5.40 x 10 ⁻⁸ ± 9.10 x 10 ⁻⁸	0.006	32	0.14
III	0.053 ± 0.0026	-5.51 x 10 ⁻⁴ ± 3.01 x 10 ⁻⁴	5.41 x 10 ⁻⁶ ± 7.35 x 10 ⁻⁶	-2.00 x 10 ⁻⁹ ± 4.80 x 10 ⁻⁸	0.006	39	0.65
IV	0.049 ± 0.0027	-1.55 x 10 ⁻⁴ ± 3.03 x 10 ⁻⁴	-3.04 x 10 ⁻⁶ ± 7.36 x 10 ⁻⁶	4.20 x 10 ⁻⁸ ± 4.80 x 10 ⁻⁸	0.006	38	0.59

Table 6 - Summary of statistical analyses of total respiratory system flow resistance during expiration data for Statistical Grouping B, comprised of the following: Group I - Control, Group II - 0.51 ppm NO₂, Group III - 0.51 mg/m³ PbCl₂, and Group IV - 0.48 ppm NO₂ + 0.54 mg/m³ PbCl₂.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	1.447 x 10 ⁻³	4.823 x 10 ⁻⁴	5.39	Yes
Error Deviation	1113	9.964 x 10 ⁻²	8.952 x 10 ⁻⁵	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.				Sy.x	n	r
	A	B	C	D			
I	0.012 ± 0.0028	-2.07 x 10 ⁻⁴ ± 3.26 x 10 ⁻⁴	-1.34 x 10 ⁻⁶ ± 7.97 x 10 ⁻⁶	2.90 x 10 ⁻⁸ ± 5.20 x 10 ⁻⁸	0.007	39	0.55
II	0.037 ± 0.0022	-2.04 x 10 ⁻⁴ ± 3.01 x 10 ⁻⁴	6.36 x 10 ⁻⁶ ± 8.97 x 10 ⁻⁶	-4.80 x 10 ⁻⁸ ± 7.10 x 10 ⁻⁸	0.005	32	0.16
III	0.046 ± 0.0023	-6.02 x 10 ⁻⁴ ± 2.70 x 10 ⁻⁴	7.29 x 10 ⁻⁶ ± 6.61 x 10 ⁻⁶	-1.90 x 10 ⁻⁸ ± 4.30 x 10 ⁻⁸	0.005	39	0.67
IV	0.042 ± 0.0025	-3.00 x 10 ⁻⁴ ± 2.86 x 10 ⁻⁴	6.46 x 10 ⁻⁶ ± 6.95 x 10 ⁻⁶	1.80 x 10 ⁻⁸ ± 4.50 x 10 ⁻⁸	0.006	38	0.60

Table 7 - Summary of statistical analyses of tidal volume data for Statistical Grouping B, comprised of the following: Group I - Control, Group II - 0.51 ppm NO₂, Group III - 0.51 mg/m³ PbClBr, and Group IV - 0.48 ppm NO₂ + 0.54 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	2.242 x 10 ²	7.474 x 10 ¹	0.61	-
Error Deviation	858	1.043 x 10 ⁵	1.216 x 10 ²	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.					SV.x	n	r
	A	B	C	D	D			
I	28.72 ± 1.92	2.52 x 10 ⁻¹ ± 1.88 x 10 ⁻¹	-2.46 x 10 ⁻³ ± 4.42 x 10 ⁻³	1.16 x 10 ⁻⁵ ± 2.84 x 10 ⁻⁵		3.48	32	0.77
II	34.13 ± 1.82	7.07 x 10 ⁻² ± 2.17 x 10 ⁻¹	7.78 x 10 ⁻⁴ ± 6.32 x 10 ⁻³	-1.02 x 10 ⁻⁵ ± 5.02 x 10 ⁻⁵		3.06	28	0.56
III	31.10 ± 1.75	1.64 x 10 ⁻² ± 1.72 x 10 ⁻¹	5.87 x 10 ⁻⁴ ± 4.10 x 10 ⁻³	3.80 x 10 ⁻⁶ ± 2.64 x 10 ⁻⁵		3.20	31	0.79
IV	28.80 ± 1.75	1.71 x 10 ⁻¹ ± 1.79 x 10 ⁻¹	-1.44 x 10 ⁻³ ± 4.20 x 10 ⁻³	7.60 x 10 ⁻⁶ ± 2.67 x 10 ⁻⁵		3.15	29	0.75

Table 8 - Summary of statistical analyses of respiratory rate data for Statistical Grouping B, comprised of the following: Group I - Control, Group II - 0.51 ppm NO₂, Group III - 0.51 mg/m³ PbClBr, and Group IV - 0.48 ppm NO₂ + 0.54 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	1.076 x 10 ³	3.586 x 10 ²	4.80	Yes
Error Deviation	858	6.411 x 10 ⁴	7.472 x 10 ¹	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.					Sy.x	n	r
	A	B	C	D	D			
I	40.74 ± 1.26	3.16 x 10 ⁻¹ ± 1.23 x 10 ⁻¹	-9.30 x 10 ⁻³ ± 2.90 x 10 ⁻³	5.63 x 10 ⁻⁵ ± 1.86 x 10 ⁻⁵		2.29	32	0.84
II	40.93 ± 1.15	4.23 x 10 ⁻³ ± 1.36 x 10 ⁻¹	-2.29 x 10 ⁻³ ± 3.97 x 10 ⁻³	1.57 x 10 ⁻⁵ ± 3.15 x 10 ⁻⁵		1.92	28	0.79
III	37.85 ± 1.83	2.67 x 10 ⁻¹ ± 1.80 x 10 ⁻¹	-4.08 x 10 ⁻³ ± 4.28 x 10 ⁻³	1.39 x 10 ⁻⁵ ± 2.76 x 10 ⁻⁵		3.34	31	0.51
IV	39.88 ± 2.03	5.14 x 10 ⁻¹ ± 2.07 x 10 ⁻¹	-1.25 x 10 ⁻² ± 4.88 x 10 ⁻³	7.67 x 10 ⁻⁵ ± 3.10 x 10 ⁻⁵		3.65	29	0.52

Table 9 - Summary of statistical analyses of dynamic compliance of the lung data for Statistical Grouping B, comprised of the following: Group I - Control, Group II - 0.51 ppm NO₂, Group III - 0.51 mg/m³ PbClBr, and Group IV - 0.48 ppm NO₂ + 0.54 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	1.481×10^1	4.937	0.97	-
Error Deviation	858	4.370×10^3	5.093	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.					n	r
	A	B	C	D	Sy.x		
I	6.01 ± 0.46	1.83×10^{-2} ± 4.55×10^{-2}	-1.88×10^{-4} ± 1.07×10^{-3}	1.30×10^{-6} ± 6.90×10^{-6}	0.94	32	0.43
II	5.90 ± 0.39	1.20×10^{-1} ± 4.63×10^{-2}	-3.08×10^{-3} ± 1.35×10^{-3}	2.19×10^{-5} ± 1.07×10^{-5}	0.65	28	0.53
III	6.09 ± 0.57	6.22×10^{-2} ± 5.65×10^{-2}	-1.12×10^{-3} ± 1.34×10^{-3}	6.80×10^{-6} ± 8.70×10^{-6}	1.05	31	0.45
IV	5.61 ± 0.46	5.95×10^{-2} ± 4.71×10^{-2}	-7.18×10^{-4} ± 1.11×10^{-3}	3.20×10^{-6} ± 7.00×10^{-6}	0.83	29	0.64

Table 10 - Summary of statistical analyses of pulmonary flow resistance data for Statistical Grouping B, comprised of the following: Group I - Control, Group II - 0.51 ppm NO₂, Group III - 0.51 mg/m³ pCIBr, and Group IV - 0.48 ppm NO₂ + 0.54 mg/m³ pCIBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	1.587 x 10 ⁻³	5.290 x 10 ⁻⁴	3.81	Yes
Error Deviation	858	1.192 x 10 ⁻¹	1.390 x 10 ⁻⁴	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.					n	r
	A	B	C	D	Sy.x		
I	0.024 ± 0.0036	7.84 x 10 ⁻⁵ ± 3.53 x 10 ⁻⁴	8.71 x 10 ⁻⁷ ± 8.32 x 10 ⁻⁶	-1.80 x 10 ⁻⁸ ± 5.30 x 10 ⁻⁸	0.006	32	0.28
II	0.026 ± 0.0025	-4.38 x 10 ⁻⁴ ± 2.99 x 10 ⁻⁴	5.68 x 10 ⁻⁶ ± 8.71 x 10 ⁻⁶	-1.50 x 10 ⁻⁸ ± 6.90 x 10 ⁻⁸	0.004	28	0.60
III	0.025 ± 0.0039	8.94 x 10 ⁻⁶ ± 3.82 x 10 ⁻⁴	-7.73 x 10 ⁻⁷ ± 9.10 x 10 ⁻⁶	-3.00 x 10 ⁻⁹ ± 5.90 x 10 ⁻⁸	0.007	31	0.45
IV	0.029 ± 0.0039	-3.96 x 10 ⁻⁴ ± 4.04 x 10 ⁻⁴	7.93 x 10 ⁻⁶ ± 9.51 x 10 ⁻⁶	-5.40 x 10 ⁻⁸ ± 6.00 x 10 ⁻⁸	0.007	29	0.51

Table 11 - Summary of statistical analyses of work of breathing during inspiration per ml tidal volume data for Statistical Grouping B, comprised of the following: Group I - Control, Group II - 0.51 ppm NO₂, Group III - 0.51 mg/m³ PbClBr, and Group IV - 0.48 ppm NO₂ + 0.54 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION

SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	2.169 x 10 ¹	7.229	4.91	Yes
Error Deviation	858	1.262 x 10 ³	1.471	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.				Sy.x	n	r
	A	B	C	D			
I	3.94 ± 0.30	-2.00 x 10 ⁻² ± 2.97 x 10 ⁻²	5.07 x 10 ⁻⁴ ± 7.00 x 10 ⁻⁴	-2.90 x 10 ⁻⁶ ± 4.50 x 10 ⁻⁶	0.55	32	0.25
II	3.37 ± 0.22	-3.85 x 10 ⁻² ± 2.61 x 10 ⁻²	1.55 x 10 ⁻³ ± 7.62 x 10 ⁻⁴	-1.27 x 10 ⁻⁵ ± 6.00 x 10 ⁻⁶	0.37	28	0.66
III	4.13 ± 0.36	-7.57 x 10 ⁻² ± 3.54 x 10 ⁻²	1.49 x 10 ⁻³ ± 8.43 x 10 ⁻⁴	-7.90 x 10 ⁻⁶ ± 5.40 x 10 ⁻⁶	0.66	31	0.46
IV	4.50 ± 0.28	-8.65 x 10 ⁻² ± 2.91 x 10 ⁻²	1.81 x 10 ⁻³ ± 6.83 x 10 ⁻⁴	-1.06 x 10 ⁻⁵ ± 4.30 x 10 ⁻⁶	0.51	29	0.58

Table 12 - Summary of statistical analyses of work of breathing during expiration per ml tidal volume data for Statistical Grouping B, comprised of the following: Group I - Control, Group II - 0.51 ppm NO₂, Group III - 0.51 mg/m³ PbClBr, and Group IV - 0.48 ppm NO₂ + 0.54 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	1.037	3.458 x 10 ⁻¹	0.87	-
Error Deviation	858	3.402 x 10 ²	3.965 x 10 ⁻¹	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.					n	r
	A	B	C	D	SY.X		
I	1.85 ± 0.16	-2.66 x 10 ⁻² ± 1.60 x 10 ⁻²	5.49 x 10 ⁻⁴ ± 3.76 x 10 ⁻⁴	-3.00 x 10 ⁻⁶ ± 2.40 x 10 ⁻⁶	0.30	32	0.36
II	1.71 ± 0.12	-1.24 x 10 ⁻² ± 1.49 x 10 ⁻²	7.00 x 10 ⁻⁴ ± 4.36 x 10 ⁻⁴	-6.70 x 10 ⁻⁶ ± 3.50 x 10 ⁻⁶	0.21	28	0.54
III	1.73 ± 0.16	-2.15 x 10 ⁻² ± 1.57 x 10 ⁻²	3.97 x 10 ⁻⁴ ± 3.74 x 10 ⁻⁴	-1.80 x 10 ⁻⁶ ± 2.40 x 10 ⁻⁶	0.29	31	0.39
IV	1.63 ± 0.18	-2.55 x 10 ⁻² ± 1.88 x 10 ⁻²	-1.10 x 10 ⁻⁵ ± 4.43 x 10 ⁻⁴	4.00 x 10 ⁻⁷ ± 2.80 x 10 ⁻⁶	0.33	29	0.17

Table 13 - Summary of statistical analyses of diffusing capacity of the lung for carbon monoxide data for Statistical Grouping B, comprised of the following: Group I - Control, Group II - 0.51 ppm NO₂, Group III - 0.51 mg/m³ PbClBr, and Group IV - 0.48 ppm NO₂ + 0.54 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ 0.05
Non-Parallelism	3	1.674 × 10 ⁻¹	5.581 × 10 ⁻²	2.36	-
Error Deviation	913	2.160 × 10 ¹	2.366 × 10 ⁻²	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.			Sy.x	n	r
	A	B	C			
I	0.62 ± 0.031	3.04 × 10 ⁻³ ± 2.91 × 10 ⁻³	-2.49 × 10 ⁻⁵ ± 7.00 × 10 ⁻⁵	1.50 × 10 ⁻⁷ ± 4.60 × 10 ⁻⁷	33	0.78
II	0.65 ± 0.041	7.80 × 10 ⁻³ ± 4.53 × 10 ⁻³	-1.43 × 10 ⁻⁴ ± 1.30 × 10 ⁻⁴	1.02 × 10 ⁻⁶ ± 1.02 × 10 ⁻⁶	29	0.75
III	0.67 ± 0.052	-3.37 × 10 ⁻³ ± 4.83 × 10 ⁻³	1.26 × 10 ⁻⁴ ± 1.16 × 10 ⁻⁴	-7.50 × 10 ⁻⁷ ± 7.70 × 10 ⁻⁷	33	0.68
IV	0.72 ± 0.041	-2.04 × 10 ⁻³ ± 3.83 × 10 ⁻³	8.80 × 10 ⁻⁵ ± 9.12 × 10 ⁻⁵	-5.90 × 10 ⁻⁷ ± 6.00 × 10 ⁻⁷	32	0.56

Table 14 - Summary of statistical analyses of number of breaths to 1% nitrogen data for Statistical Grouping B, comprised of the following: Group I - Control, Group II - 0.51 ppm NO₂, Group III - 0.51 mg/m³ PbClBr, and Group IV - 0.48 ppm NO₂ + 0.54 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	3.902 x 10 ²	1.301 x 10 ²	0.70	-
Error Deviation	887	1.650 x 10 ⁵	1.860 x 10 ²	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.					n	r
	A	B	C	D	Sy.x		
I	42.65 ± 3.42	8.85 x 10 ⁻² ± 3.26 x 10 ⁻¹	1.08 x 10 ⁻³ ± 7.83 x 10 ⁻¹	2.10 x 10 ⁻⁵ ± 5.20 x 10 ⁻⁵	5.69	32	0.33
II	36.69 ± 2.64	3.21 x 10 ⁻¹ ± 2.90 x 10 ⁻¹	-7.83 x 10 ⁻³ ± 8.28 x 10 ⁻³	5.40 x 10 ⁻⁵ ± 6.50 x 10 ⁻⁵	4.16	28	0.26
III	44.77 ± 3.08	2.51 x 10 ⁻¹ ± 2.93 x 10 ⁻¹	1.16 x 10 ⁻³ ± 7.06 x 10 ⁻³	-3.40 x 10 ⁻⁵ ± 4.70 x 10 ⁻⁵	5.16	32	0.64
IV	47.50 ± 3.43	2.37 x 10 ⁻¹ ± 3.32 x 10 ⁻¹	-4.11 x 10 ⁻⁴ ± 7.93 x 10 ⁻³	-1.80 x 10 ⁻⁵ ± 5.20 x 10 ⁻⁵	5.70	31	0.49

Table 15 - Summary of statistical analyses of respiratory rate (during oxygen breathing) data for Statistical Grouping B, comprised of the following: Group I - Control, Group II - 0.51 ppm NO₂, Group III - 0.51 mg/m³ PbClBr, and Group IV - 0.48 ppm NO₂ + 0.54 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	4.593 x 10 ²	1.531 x 10 ²	1.70	-
Error Deviation	887	7.964 x 10 ⁴	8.979 x 10 ¹	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.					SY.X	n	r
	A	B	C	D				
I	34.46 ± 1.11	2.49 x 10 ⁻¹ ± 1.06 x 10 ⁻¹	-9.27 x 10 ⁻³ ± 2.54 x 10 ⁻³	6.52 x 10 ⁻⁵ ± 1.68 x 10 ⁻⁵		1.84	32	0.86
II	36.57 ± 1.17	-8.90 x 10 ⁻² ± 1.29 x 10 ⁻¹	2.02 x 10 ⁻³ ± 3.67 x 10 ⁻³	-2.20 x 10 ⁻⁵ ± 2.88 x 10 ⁻⁵		1.84	28	0.71
III	33.38 ± 1.80	1.91 x 10 ⁻¹ ± 1.71 x 10 ⁻¹	-2.86 x 10 ⁻³ ± 4.13 x 10 ⁻³	7.40 x 10 ⁻⁶ ± 2.72 x 10 ⁻⁵		3.02	32	0.52
IV	35.78 ± 2.53	5.96 x 10 ⁻¹ ± 2.45 x 10 ⁻¹	-1.18 x 10 ⁻² ± 5.85 x 10 ⁻³	5.88 x 10 ⁻⁵ ± 3.83 x 10 ⁻⁵		4.20	31	0.61

Table 16 - Summary of statistical analyses of cumulative tidal volume to 1% nitrogen data for Statistical Grouping B, comprised of the following: Group I - Control; Group II - 0.51 ppm NO₂, Group III - 0.51 mg/m³ PbClBr, and Group IV - 0.48 ppm NO₂ + 0.54 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	3.368 x 10 ⁻¹	1.123 x 10 ⁻¹	0.64	-
Error Deviation	887	1.557 x 10 ²	1.756 x 10 ⁻¹	-	-

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THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.				Sy.x	n	r
	A	B	C	D			
I	1.35 ± 0.094	5.79 x 10 ⁻³ ± 8.95 x 10 ⁻⁴	-1.38 x 10 ⁻⁵ ± 2.15 x 10 ⁻⁴	0.00 ± 1.40 x 10 ⁻⁶	0.16	32	0.70
II	1.19 ± 0.119	-3.08 x 10 ⁻³ ± 1.31 x 10 ⁻²	2.56 x 10 ⁻⁴ ± 3.74 x 10 ⁻⁴	-2.40 x 10 ⁻⁶ ± 2.90 x 10 ⁻⁶	0.19	28	0.46
III	1.52 ± 0.074	4.55 x 10 ⁻⁴ ± 7.05 x 10 ⁻³	2.09 x 10 ⁻⁴ ± 1.70 x 10 ⁻⁴	-1.80 x 10 ⁻⁶ ± 1.10 x 10 ⁻⁶	0.12	32	0.82
IV	1.44 ± 0.112	-1.16 x 10 ⁻³ ± 1.09 x 10 ⁻²	2.78 x 10 ⁻⁴ ± 2.60 x 10 ⁻⁴	-2.50 x 10 ⁻⁶ ± 1.70 x 10 ⁻⁶	0.19	31	0.68

Table 17 - Summary of statistical analyses of tidal volume (during oxygen breathing) data for Statistical Grouping B, comprised of the following: Group I - Control; Group II - 0.51 ppm NO₂, Group III - 0.51 mg/m³ PbClBr, and Group IV - 0.48 ppm NO₂ + 0.54 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	4.624 x 10 ²	1.541 x 10 ²	1.56	-
Error Deviation	887	8.777 x 10 ⁴	9.895 x 10 ¹	-	-

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THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.					SV.X	n	r
	A	B	C	D				
I	39.08 ± 2.58	2.20 x 10 ⁻¹ ± 2.47 x 10 ⁻¹	-5.34 x 10 ⁻³ ± 5.92 x 10 ⁻³	4.68 x 10 ⁻⁵ ± 3.91 x 10 ⁻⁵		4.30	32	0.70
II	40.72 ± 3.73	-4.24 x 10 ⁻¹ ± 4.09 x 10 ⁻¹	1.68 x 10 ⁻² ± 1.17 x 10 ⁻²	-1.39 x 10 ⁻⁴ ± 9.15 x 10 ⁻⁵		5.87	28	0.47
III	43.09 ± 2.17	-1.77 x 10 ⁻¹ ± 2.07 x 10 ⁻¹	3.84 x 10 ⁻³ ± 4.97 x 10 ⁻³	-1.63 x 10 ⁻⁵ ± 3.28 x 10 ⁻⁵		3.64	32	0.53
IV	38.50 ± 2.39	-2.36 x 10 ⁻¹ ± 2.32 x 10 ⁻¹	7.94 x 10 ⁻³ ± 5.54 x 10 ⁻³	-5.38 x 10 ⁻⁵ ± 3.63 x 10 ⁻⁵		3.98	31	0.53

Table 18 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for hematocrit (Hct. - percent) for male and female monkeys in Statistical Grouping B.

Groups	Pre-exposure -8	Time-Weeks			
		4	16	40	68
I - Control	36.4 (0.8)	35.0 (1.0)	33.1 (1.0)	35.4 (0.8)	37.3 (1.0)
II - 0.51 ppm NO ₂	37.3 (0.8)	37.3 (0.7)	38.4 (0.9)	37.0 (1.1)	38.8 (1.2)
III - 0.51 mg/m ³ PbClBr	32.3 (0.8)	35.8 (0.8)	34.3 (0.9)	33.6 (0.9)	35.4 (1.1)
IV - 0.48 ppm NO ₂ + 0.54 mg/m ³ PbClBr	34.7 (0.7)	35.9 (0.5)	34.4 (0.7)	34.9 (0.7)	35.1 (0.7)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Pre-exposure -8	Time-Weeks			
		4	16	40	68
Pb	SIG	N.S.	N.S.	SIG	N.S.
NO ₂	SIG	N.S.	SIG	N.S.	N.S.
Interaction	N.S.	N.S.	SIG	N.S.	N.S.

Table 19 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for hemoglobin (Hgb. - grams percent) for male and female monkeys in Statistical Grouping B.

Groups	Time-Weeks				
	Pre-exposure -8	4	16	40	68
I - Control					
	10.5 (0.3)	11.0 (0.3)	11.2 (0.2)	11.0 (0.3)	10.7 (0.3)
II - 0.51 ppm NO ₂					
	11.1 (0.3)	10.8 (0.2)	11.2 (0.3)	11.4 (0.4)	12.5 (0.4)
III - 0.51 mg/m ³ PbClBr					
	10.2 (0.2)	9.8 (0.2)	10.4 (0.2)	9.1 (0.2)	10.4 (0.3)
IV - 0.48 ppm NO ₂ + 0.54 mg/m ³ PbClBr					
	10.3 (0.2)	10.1 (0.2)	10.5 (0.3)	10.2 (0.3)	10.2 (0.3)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks				
	Pre-exposure -8	4	16	40	68
Pb	SIG	SIG	SIG	SIG	SIG
NO ₂	N.S.	N.S.	N.S.	SIG	N.S.
Interaction	N.S.	N.S.	N.S.	N.S.	SIG

Table 20 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for total erythrocyte count (RBC - 106/cmm) for male and female monkeys in Statistical Grouping B.

Groups	Time-Weeks					
	Pre-exposure -8	4	16	40	68	104
I - Control	5.44 (0.09)	5.44 (0.18)	5.70 (0.22)	5.29 (0.18)	5.10 (0.13)	6.13 (0.14)
II - 0.51 ppm NO ₂	4.81 (0.15)	4.83 (0.14)	5.07 (0.14)	4.69 (0.14)	5.39 (0.18)	5.17 (0.16)
III - 0.51 mg/m ³ PbClBr	5.13 (0.18)	4.89 (0.20)	5.39 (0.30)	5.19 (0.19)	5.64 (0.23)	5.80 (0.19)
IV - 0.48 ppm NO ₂ + 0.54 mg/m ³ PbClBr	4.66 (0.17)	4.67 (0.14)	5.16 (0.18)	4.95 (0.18)	5.46 (0.17)	5.84 (0.21)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks					
	Pre-exposure -8	4	16	40	68	104
Pb	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.
NO ₂	SIG	SIG	N.S.	SIG	N.S.	SIG
Interaction	N.S.	N.S.	N.S.	N.S.	N.S.	SIG

Table 21 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for total leukocyte count (WBC - per cmm) for male and female monkeys in Statistical Grouping B.

Groups	Time-Weeks						
	Pre-exposure	-8	4	16	40	68	104
I - Control	7240 (340)		7170 (290)	8670 (710)	10620 (850)	8220 (680)	11940 (1110)
II - 0.51 ppm NO ₂	10250 (620)		10460 (890)	11380 (890)	8360 (1040)	7730 (710)	9640 (980)
III - 0.51 mg/m ³ PbClBr	8430 (860)		11040 (3060)	9700 (930)	8860 (830)	5110 (850)	8420 (870)
IV - 0.48 ppm NO ₂ + 0.54 mg/m ³ PbClBr	8740 (850)		6300 (630)	7280 (440)	7400 (600)	7320 (640)	7270 (540)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks						
	Pre-exposure	-8	4	16	40	68	104
Pb	N.S.		N.S.	N.S.	N.S.	N.S.	SIG
NO ₂	N.S.		N.S.	N.S.	SIG	N.S.	N.S.
Interaction	N.S.		SIG	SIG	N.S.	N.S.	N.S.

Table 23 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for blood urea nitrogen (BUN - mg percent) for male and female monkeys in Statistical Grouping B.

Groups	Time-Weeks			
	Pre-exposure -8	4	16	68
I - Control	16.3 (1.0)	19.2 (1.4)	17.0 (0.6)	22.6 (0.7)
II - 0.51 ppm NO ₂	19.9 (1.2)	15.8 (1.5)	18.9 (1.4)	20.6 (1.0)
III - 0.51 mg/m ³ PbClBr	14.4 (0.6)	15.8 (0.5)	8.8 (0.9)	22.6 (1.6)
IV - 0.48 ppm I ₂ O ₅ + 0.54 mg/m ³ PbClBr	15.0 (1.4)	14.8 (1.4)	15.0 (1.8)	20.7 (1.4)
				23.2 (1.1)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks			
	Pre-exposure -8	4	16	68
Pb	SIG	N.S.	SIG	SIG
NO ₂	N.S.	N.S.	SIG	N.S.
Interaction	N.S.	N.S.	N.S.	SIG

Table 22 - Mean values $\pm$ and summary of factorial analysis of variance for blood glucose (Glu. - mg percent) for male and female monkeys in Statistical Grouping B.

Groups	Time-Weeks				
	Pre-exposure -8	4	16	40	68
I - Control	59.3 (3.3)	59.5 (3.3)	69.0 (4.4)	94.6 (4.3)	97.3 (5.3)
II - 0.51 ppm NO ₂	80.5 (3.9)	75.8 (3.2)	93.8 (7.1)	77.7 (3.7)	78.1 (8.6)
III - 0.51 mg/m ³ PbClBr	83.3 (2.9)	52.0 (3.0)	80.0 (2.2)	59.3 (4.4)	93.4 (3.5)
IV - 0.48 ppm NO ₂ + 0.54 mg/m ³ PbClBr	80.1 (12.3)	56.3 (3.4)	68.0 (3.7)	82.2 (7.8)	104.2 (6.7)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks				
	Pre-exposure -8	4	16	40	68
Pb	N.S.	SIG	N.S.	N.S.	N.S.
NO ₂	SIG	SIG	N.S.	N.S.	N.S.
Interaction	N.S.	N.S.	SIG	SIG	SIG

Table 22 - Mean values $\pm$ and summary of factorial analysis of variance for blood glucose (Glu. - mg percent) for male and female monkeys in Statistical Grouping B.

Groups	Time-Weeks				
	Pre-exposure -8	4	16	40	68
I - Control	59.3 (3.3)	59.5 (3.3)	69.0 (4.4)	94.6 (4.3)	97.3 (5.3)
II - 0.51 ppm NO ₂	80.5 (3.9)	75.8 (3.2)	93.8 (7.1)	77.7 (3.7)	78.1 (8.6)
III - 0.51 mg/m ³ PbClBr	68.3 (2.9)	52.0 (3.0)	80.0 (2.2)	69.3 (4.4)	93.4 (3.5)
IV - 0.48 ppm NO ₂ + 0.54 mg/m ³ PbClBr	80.1 (12.3)	56.3 (3.4)	68.0 (3.7)	82.2 (7.8)	104.2 (6.7)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks				
	Pre-exposure -8	4	16	40	68
Pb	N.S.	SIG	N.S.	N.S.	N.S.
NO ₂	SIG	SIG	N.S.	N.S.	N.S.
Interaction	N.S.	N.S.	SIG	SIG	SIG

Table 23 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for blood urea nitrogen (BUN - mg percent) for male and female monkeys in Statistical Grouping 8.

Groups	Time-Weeks			
	Pre-exposure -8	4	16	68
I - Control	16.3 (1.0)	19.2 (1.4)	17.0 (0.6)	23.2 (1.1)
II - 0.51 ppm NO ₂	19.9 (1.2)	15.8 (1.5)	18.9 (1.4)	20.6 (1.0)
III - 0.51 mg/m ³ PbClBr	14.4 (0.6)	15.8 (0.5)	8.8 (0.9)	19.8 (1.1)
IV - 0.45 ppm NO ₂ + 0.54 mg/m ³ PbClBr	15.0 (1.4)	14.8 (1.4)	15.0 (1.8)	22.3 (1.7)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks			
	Pre-exposure -8	4	16	68
Pb	SIG	N.S.	SIG	SIG
NO ₂	N.S.	N.S.	SIG	SIG
Interaction	N.S.	N.S.	N.S.	SIG

Table 24 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for total serum bilirubin (mg percent) for male and female monkeys in Statistical Grouping B.

Groups	Time-Weeks				
	Pre-exposure -8	4	16	40	68
I - Control	0.27 (0.03)	0.25 (0.02)	0.26 (0.02)	0.31 (0.02)	0.29 (0.03)
II - 0.51 ppm NO ₂	0.22 (0.00)	0.22 (0.02)	0.32 (0.01)	0.30 (0.01)	0.37 (0.01)
III - 0.51 mg/m ³ PbClBr	0.18 (0.01)	0.28 (0.02)	0.28 (0.02)	0.40 (0.02)	0.27 (0.01)
IV - 0.48 ppm NO ₂ + 0.54 mg/m ³ PbClBr	0.26 (0.04)	0.29 (0.03)	0.28 (0.01)	0.27 (0.01)	0.39 (0.11)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks				
	Pre-exposure -8	4	16	40	68
Pb	N.S.	N.S.	N.S.	N.S.	N.S.
NO ₂	N.S.	N.S.	N.S.	SIG	N.S.
Interaction	SIG	N.S.	N.S.	SIG	N.S.

Table 25 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for total serum protein (grams percent) for male and female monkeys in Statistical Grouping B.

Groups	Time-Weeks				
	Pre-exposure -8	4	16	40	68
I - Control	7.30 (0.13)	7.76 (0.13)	8.24 (0.10)	7.89 (0.21)	7.44 (0.13)
II - 0.51 ppm NO ₂	7.25 (0.13)	7.56 (0.10)	7.52 (0.12)	7.50 (0.10)	7.45 (0.10)
III - 0.51 mg/m ³ PbClBr	7.53 (0.17)	7.74 (0.19)	7.75 (0.22)	7.19 (0.12)	7.00 (0.13)
IV - 0.48 ppm NO ₂ + 0.54 mg/m ³ PbClBr	7.17 (0.19)	7.38 (0.11)	7.38 (0.14)	7.36 (0.10)	6.97 (0.12)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks				
	Pre-exposure -8	4	16	40	68
Pb	N.S.	N.S.	N.S.	SIG	SIG
NO ₂	N.S.	N.S.	SIG	N.S.	SIG
Interaction	N.S.	N.S.	N.S.	SIG	N.S.

Table 26 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for serum albumin (grams percent) for male and female monkeys in Statistical Grouping B.

Groups	Time-Weeks				
	Pre-exposure -8	4	16	40	68
I - Control	2.56 (0.14)	2.58 (0.05)	3.11 (0.06)	2.87 (0.08)	2.45 (0.11)
II - 0.51 ppm NO ₂	2.75 (0.09)	2.76 (0.08)	2.96 (0.05)	3.13 (0.08)	3.19 (0.10)
III - 0.51 mg/m ³ PbClBr	2.41 (0.05)	2.80 (0.05)	2.49 (0.04)	2.37 (0.05)	2.56 (0.05)
IV - 0.48 ppm NO ₂ + 0.54 mg/m ³ PbClBr	2.45 (0.09)	3.09 (0.09)	2.58 (0.08)	2.69 (0.09)	2.80 (0.12)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks				
	Pre-exposure -8	4	16	40	68
Pb	SIG	SIG	SIG	SIG	N.S.
NO ₂	N.S.	SIG	N.S.	SIG	SIG
Interaction	N.S.	N.S.	N.S.	N.S.	SIG

Table 27 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for serum sodium (Na - mEq/liter) for male and female monkeys in Statistical Grouping B.

Groups	Time-Weeks					
	Pre-exposure -8	4	16	40	68	104
I - Control	148.0 (0.5)	143.7 (0.3)	139.2 (0.6)	148.7 (0.5)	145.8 (0.8)	148.7 (0.6)
II - 0.51 ppm NO ₂	147.0 (0.5)	143.1 (0.3)	148.6 (1.0)	145.4 (0.5)	147.5 (0.4)	145.6 (0.3)
III - 0.51 mg/m ³ PbClBr	147.1 (0.4)	145.0 (0.6)	141.8 (0.5)	143.0 (0.2)	148.0 (0.8)	148.5 (0.5)
IV - 0.48 ppm NO ₂ + 0.54 mg/m ³ PbClBr	147.7 (0.7)	136.5 (2.3)	143.0 (0.3)	142.4 (0.7)	149.7 (0.7)	146.6 (0.2)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks					
	Pre-exposure -3	4	16	40	68	104
Pb	N.S.	N.S.	SIG	SIG	SIG	N.S.
NO ₂	N.S.	SIG	SIG	SIG	SIG	SIG
Interaction	N.S.	SIG	SIG	SIG	N.S.	N.S.

Table 23 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for serum potassium (K-mEq/liter) for male and female monkeys in Statistical Grouping B.

Groups	Time-Weeks				
	Pre-exposure -8	4	16	40	68
I - Control	3.75 (0.24)	3.67 (0.20)	3.64 (0.21)	3.80 (0.12)	4.02 (0.10)
II - 0.51 ppm NO ₂	3.93 (0.11)	4.15 (0.08)	3.80 (0.10)	3.68 (0.11)	3.72 (0.10)
III - 0.51 mg/m ³ PbClBr	3.62 (0.09)	3.76 (0.24)	3.86 (0.18)	3.89 (0.11)	3.86 (0.15)
IV - 0.48 ppm NO ₂ + 0.54 mg/m ³ PbClBr	4.05 (0.17)	3.68 (0.16)	3.73 (0.11)	3.95 (0.09)	4.30 (0.21)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks				
	Pre-exposure -8	4	16	40	68
Pb	N.S.	N.S.	N.S.	N.S.	SIG
NO ₂	N.S.	N.S.	N.S.	N.S.	N.S.
Interaction	N.S.	N.S.	N.S.	N.S.	SIG

Table 29 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for serum chlorides (Cl - mEq/liter) for male and female monkeys in Statistical Grouping B.

Groups	Time-Weeks					
	Pre-exposure	-8	4	16	40	68
I - Control	112.0 (1.1)	109.67 (0.6)	108.4 (1.0)	107.7 (0.8)	110.2 (0.8)	112.8 (1.3)
II - 0.51 ppm NO ₂	105.2 (0.8)	113.1 (0.6)	109.7 (0.7)	107.5 (0.3)	108.3 (0.6)	106.8 (0.6)
III - 0.51 mg/m ³ PbClBr	112.9 (0.5)	103.2 (0.4)	109.9 (0.6)	114.7 (0.7)	111.5 (0.8)	112.3 (0.4)
IV - 0.48 ppm NO ₂ + 0.54 mg/m ³ PbClBr	110.4 (0.9)	104.5 (0.5)	110.5 (0.8)	111.3 (0.4)	112.6 (0.9)	113.8 (0.2)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks						
	Pre-exposure	-8	4	16	40	68	104
Pb	SIG		SIG	N.S.	SIG	SIG	SIG
NO2	SIG		SIG	N.S.	SIG	N.S.	SIG
Interaction	SIG		N.S.	N.S.	SIG	N.S.	SIG

Table 30 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for serum carbon dioxide (CO_2 - mEq/liter) for male and female monkeys in Statistical Grouping B.

Groups	Time-Weeks						
	Pre-exposure	-8	4	16	40	68	104
I - Control	24.8 (1.0)		24.3 (0.8)	28.9 (0.7)	27.6 (0.5)	26.4 (0.7)	25.8 (0.6)
II - 0.51 ppm NO ₂	27.8 (1.0)		25.2 (0.9)	25.7 (1.1)	24.7 (0.5)	28.8 (1.1)	24.2 (1.0)
III - 0.51 mg/m ³ PbClBr	26.7 (0.6)		25.7 (0.9)	22.9 (1.7)	29.4 (1.0)	26.5 (0.5)	24.6 (1.4)
IV - 0.48 ppm NO ₂ + 0.54 mg/m ³ PbClBr	26.2 (0.7)		25.1 (0.3)	25.7 (0.6)	27.5 (1.1)	26.2 (0.5)	24.9 (0.6)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks						
	Pre-exposure	-8	4	16	40	68	104
Pb	N.S.	N.S.	N.S.	SIG	SIG	N.S.	N.S.
NO2	N.S.	N.S.	N.S.	N.S.	SIG	N.S.	N.S.
Interaction	N.S.	N.S.	N.S.	SIG	N.S.	N.S.	N.S.

Table 3) - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for serum calcium (Ca - mg percent) for male and female monkeys in Statistical Grouping B.

Groups	Time-Weeks				
	Pre-exposure -8	4	16	40	68
I - Control	9.47 (0.22)	9.36 (0.11)	10.16 (0.08)	11.14 (0.09)	9.55 (0.30)
II - 0.51 ppm NO ₂	9.89 (0.27)	10.34 (0.25)	10.19 (0.22)	9.68 (0.10)	9.54 (0.12)
III - 0.51 mg/m ³ PbCl ₂	9.77 (0.13)	9.33 (0.11)	9.35 (0.22)	10.03 (0.15)	9.90 (0.12)
IV - 0.48 ppm NO ₂ + 0.54 mg/m ³ PbCl ₂	9.15 (0.19)	9.54 (0.13)	9.49 (0.18)	10.64 (0.14)	10.22 (0.14)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks				
	Pre-exposure -8	4	16	40	68
Pb	N.S.	SIG	SIG	N.S.	SIG
NO ₂	N.S.	SIG	N.S.	SIG	N.S.
Interaction	SIG	SIG	N.S.	SIG	N.S.

Table 32 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for serum glutamic oxaloacetic transaminase (SGOT - K units) for male and female monkeys in Statistical Grouping B.

Groups	Time-Weeks				
	Pre-exposure -8	4	16	40	68
I - Control	26.0 (4.8)	45.4 (7.1)	20.2 (0.8)	33.6 (3.5)	97.3 (21.3)
II - 0.51 ppm NO ₂	50.0 (9.8)	51.5 (6.2)	58.2 (5.7)	58.0 (2.2)	52.9 (4.1)
III - 0.51 mg/m ³ PbClBr	30.2 (2.1)	31.6 (2.2)	57.0 (10.7)	47.2 (7.8)	53.3 (4.5)
IV - 0.48 ppm NO ₂ + 0.54 mg/m ³ PbClBr	36.2 (3.0)	33.0 (1.9)	38.4 (6.3)	37.4 (1.6)	83.6 (16.1)
					44.7 (4.8)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks				
	Pre-exposure -8	4	16	40	68
Pb	N.S.	SIG	N.S.	N.S.	SIG
NO ₂	SIG	N.S.	N.S.	N.S.	SIG
Interaction	N.S.	N.S.	SIG	SIG	SIG

Table 33 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for serum glutamic pyruvic transaminase (SGPT - RF units) for male and female monkeys in Statistical Grouping B.

Groups	Time-Weeks				
	Pre-exposure -8	4	16	40	68
I - Control	15.4 (2.8)	20.7 (3.0)	25.1 (2.7)	41.3 (8.6)	41.4 (2.8)
II - 0.51 ppm NO ₂	49.3 (12.7)	38.2 (2.5)	76.2 (14.0)	52.3 (10.5)	84.8 (13.7)
III - 0.51 mg/m ³ PbClBr	26.3 (2.5)	27.7 (1.5)	20.2 (3.0)	29.5 (5.0)	47.4 (0.7)
IV - 0.48 ppm NO ₂ + 0.54 mg/m ³ PbClBr	33.9 (2.0)	28.3 (2.0)	16.7 (2.4)	37.9 (4.0)	47.2 (0.7)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks				
	Pre-exposure -8	4	16	40	68
Po	N.S.	N.S.	SIG	N.S.	SIG
NO ₂	SIG	SIG	SIG	N.S.	SIG
Interaction	SIG	SIG	SIG	N.S.	SIG

Table 34 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for lactic acid dehydrogenase (LDH - WROB units) for male and female monkeys in Statistical Grouping B.

Groups	Pre-exposure -8	Time-Weeks			
		4	16	40	68
I - Control	512 (99)	746 (48)	572 (80)	833 (220)	1573 (156)
II - 0.51 ppm NO ₂	578 (47)	659 (86)	627 (106)	602 (87)	320 (47)
III - 0.51 mg/m ³ PbClBr	926 (56)	794 (82)	822 (173)	663 (69)	1306 (129)
IV - 0.48 ppm NO ₂ + 0.54 mg/m ³ PbClBr	748 (108)	807 (78)	600 (75)	433 (64)	1480 (195)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Pre-exposure -8	Time-Weeks			
		4	16	40	68
Pb	SIG	N.S.	N.S.	N.S.	SIG
NO ₂	N.S.	N.S.	N.S.	N.S.	SIG
Interaction	N.S.	N.S.	N.S.	N.S.	SIG

Table 35 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for alkaline phosphatase (Alk. P₀₄ - KA units) for male and female monkeys in Statistical Grouping B.

Groups	Time-Weeks					
	Pre-exposure -8	4	16	40	68	104
I - Control	57.2 (17.3)	58.6 (8.8)	55.3 (8.3)	48.4 (5.3)	41.9 (7.3)	48.4 (8.6)
II - 0.51 ppm NO ₂	55.7 (13.6)	61.2 (13.0)	59.8 (10.5)	40.4 (8.4)	34.3 (6.9)	31.4 (7.9)
III - 0.51 mg/m ³ PbClBr	54.4 (8.6)	50.7 (6.9)	67.5 (9.9)	56.3 (10.8)	49.2 (8.4)	41.4 (7.6)
IV - 0.48 ppm NO ₂ + 0.54 mg/m ³ PbClBr	62.1 (6.4)	62.8 (3.0)	79.6 (9.8)	69.6 (10.1)	54.2 (7.1)	47.0 (5.6)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks					
	Pre-exposure -8	4	16	40	68	104
Pb	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.
NO2	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.
Interaction	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.

Table 36 - Mean values $\pm$ (S.E.) for blood gas and pH variables measured in male and female monkeys in Statistical Grouping B, comprised of the following: Group I - Control, Group II - 0.51 ppm NO₂, Group III - 0.51 mg/m³ PbClBr, and Group IV - 0.48 ppm NO₂ + 0.54 mg/m³ PbClBr.

Interval Week	PO ₂				PCO ₂				pH			
	Group I	Group II	Group III	Group IV	Group I	Group II	Group III	Group IV	Group I	Group II	Group III	Group IV
-3	91.6 (2.0)	84.3 (0.7)	87.4 (1.7)	85.8 (1.9)	39.9 (0.7)	39.4 (0.9)	41.0 (0.8)	42.2 (1.1)	7.38 (0.00)	7.39 (0.01)	-	-
1	87.8 (1.8)	87.6 (1.1)	91.9 (2.7)	87.4 (2.0)	37.2 (1.0)	40.6 (1.1)	43.8 (1.2)	43.0 (0.8)	7.37 (0.00)	7.36 (0.01)	7.35 (0.01)	7.35 (0.01)
6	87.8 (1.9)	84.0 (1.0)	88.5 (1.9)	90.4 (1.6)	44.4 (1.0)	40.3 (1.0)	37.9 (1.1)	40.7 (1.3)	-	7.36 (0.01)	7.37 (0.00)	7.37 (0.01)
13	87.5 (0.9)	84.8 (1.7)	90.5 (1.3)	89.4 (1.8)	39.8 (1.3)	42.5 (0.8)	38.2 (1.1)	39.0 (1.1)	7.37 (0.00)	7.37 (0.01)	7.37 (0.01)	7.40 (0.00)
26	89.6 (1.9)	87.7 (2.0)	84.5 (1.1)	84.1 (0.9)	40.3 (1.2)	45.3 (0.8)	38.7 (0.6)	38.6 (1.0)	7.38 (0.01)	7.38 (0.00)	7.37 (0.01)	7.38 (0.00)
39	85.8 (1.2)	96.8 (1.5)	88.4 (1.1)	85.9 (1.1)	40.4 (1.8)	52.7 (1.0)	37.4 (1.3)	40.0 (0.7)	7.38 (0.00)	7.36 (0.00)	7.35 (0.01)	7.35 (0.00)
65	86.5 (1.6)	-	86.5 (1.7)	90.3 (1.6)	46.1 (1.6)	-	47.4 (0.8)	47.6 (1.3)	7.38 (0.00)	-	7.36 (0.00)	7.34 (0.01)
78	91.6 (1.6)	83.6 (1.3)	97.7 (2.8)	94.7 (2.9)	42.2 (1.4)	43.7 (0.8)	51.9 (1.1)	51.8 (2.9)	7.35 (0.01)	7.35 (0.01)	7.34 (0.01)	7.38 (0.00)
91	98.7 (2.6)	84.5 (1.2)	94.5 (2.4)	90.9 (2.7)	51.1 (2.4)	41.2 (1.2)	49.8 (1.5)	45.3 (0.7)	7.37 (0.01)	7.33 (0.02)	7.39 (0.01)	7.37 (0.00)
104	96.4 (2.2)	-	83.7 (1.0)	87.2 (1.7)	39.8 (1.5)	-	39.1 (0.9)	36.7 (1.4)	7.36 (0.01)	-	7.34 (0.00)	7.33 (0.01)

Table 37 - Mean values $\pm$ (S.D.) and summary of single classification analysis of variance for terminal body weight (g.), organ weight (g.), and organ/body weight ratios (%) for male monkeys for Statistical Grouping B, comprised of the following: Group I - Control, Group II - 0.51 ppm NO₂, Group III - 0.51 mg/m³ PbClBr, and Group IV - 0.48 ppm NO₂ + 0.54 mg/m³ PbClBr.

Groups	Terminal Body Weight	Brain		Thyroid		Lung		Heart		Liver		Kidneys		Adrenals	
		wt.	ratio	wt.*	ratio	wt.	ratio	wt.	ratio*	wt.	ratio	wt.	ratio	wt.*	ratio
I	4920 (1410)	73.8 (7.7)	1.57 (0.31)	0.53 (0.34)	0.010 (0.004)	27.8 (6.0)	0.58 (0.08)	16.6 (4.6)	0.34 (0.05)	88.1 (13.3)	1.85 (0.25)	18.6 (4.6)	0.38 (0.05)	0.63 (0.13)	0.013 (0.002)
II	4525 (585)	67.8 (7.7)	1.52 (0.30)	0.38 (0.10)	0.008 (0.001)	26.1 (5.5)	0.59 (0.17)	14.3 (1.8)	0.32 (0.05)	72.8 (8.6)	1.62 (0.26)	15.0 (1.7)	0.34 (0.05)	0.52 (0.04)	0.012 (0.002)
III	4/20 (2252)	67.3 (3.5)	1.59 (0.45)	0.41 (0.13)	0.009 (0.003)	28.2 (9.9)	0.62 (0.07)	16.4 (7.4)	0.35 (0.01)	84.8 (26.6)	1.88 (0.27)	18.3 (7.6)	0.39 (0.05)	0.76 (0.35)	0.016 (0.003)
IV	4880 (2099)	51.0 (3.7)	1.43 (0.53)	0.38 (0.05)	0.008 (0.002)	23.8 (4.8)	0.52 (0.11)	16.9 (7.0)	0.35 (0.01)	88.0 (17.2)	1.94 (0.40)	18.1 (3.4)	0.40 (0.10)	0.69 (0.14)	0.015 (0.005)
Significant Differences (p $\leq$.05)															
I vs II	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.
I vs III	N.S.	H.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.
I vs IV	N.S.	SIG	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.
II vs III	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.
II vs IV	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	SIG	N.S.
III vs IV	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.

* The variances of these groups were heterogeneous.

Table 38 - Mean values $\pm$ (S.D.) and summary of single classification analysis of variance for terminal body weight (g.), organ weight (g.), and organ/body weight ratios (%) for female monkeys of Statistical Grouping B, comprised of the following: Group I - Control, Group II - 0.51 ppm NO₂, Group III - 0.51 mg/m³ PbClBr, and Group IV - 0.48 ppm NO₂ + 0.54 mg/m³ PbClBr.

Groups	Terminal Body Weight	Brain		Thyroid		Lung		Heart		Liver		Kidneys		Adrenals	
		wt.	ratio	wt.	ratio	wt.	ratio	wt.	ratio	wt.	ratio	wt.	ratio	wt.*	ratio*
I	3075 (205)	59.5 (3.1)	1.94 (0.13)	0.43 (0.09)	0.014 (0.004)	21.6 (2.4)	0.70 (0.06)	9.7 (0.8)	0.31 (0.01)	66.3 (4.4)	2.16 (0.17)	13.2 (1.4)	0.43 (0.04)	0.76 (0.29)	0.025 (0.010)
II	3140 (288)	57.8 (4.1)	1.85 (0.17)	0.34 (0.11)	0.011 (0.004)	22.4 (3.0)	0.72 (0.10)	10.0 (1.0)	0.32 (0.03)	63.9 (10.4)	2.03 (0.17)	13.3 (1.2)	0.42 (0.04)	0.50 (0.01)	0.016 (0.001)
III	2750 (342)	58.9 (6.3)	2.16 (0.32)	0.30 (0.11)	0.011 (0.004)	20.7 (2.8)	0.75 (0.05)	10.2 (2.7)	0.37 (0.05)	59.0 (9.7)	2.14 (0.14)	13.7 (1.8)	0.50 (0.05)	0.69 (0.13)	0.025 (0.002)
IV	3125 (206)	59.5 (6.9)	1.90 (0.13)	0.40 (0.09)	0.013 (0.004)	22.4 (4.7)	0.72 (0.16)	10.8 (1.2)	0.34 (0.02)	75.2 (4.1)	2.41 (0.12)	16.3 (3.1)	0.52 (0.12)	0.58 (0.09)	0.018 (0.003)

Significant Differences ($p \leq 0.05$)

I vs II	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.
I vs III	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.
I vs IV	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.
II vs III	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	SIG	SIG
II vs IV	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	SIG	N.S.	N.S.	N.S.	N.S.
III vs IV	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	SIG

* The variances of these groups were heterogeneous.

Table 39 - Histopathology incidence table for Statistical Grouping B, comprised of the following: Group I - Control, Group II - 0.51 ppm NO₂, Group III - 0.51 mg/m³ PbCl₂Br, and Group IV - 0.48 ppm NO₂ + 0.54 mg/m³ PbCl₂Br.

	GROUPS			
	I	II	III	IV
LUNG				
Focal Pleural Thickening	2/9	0/9	2/9	3/9
Peribronchial Brown Pigment	1/9	1/9	3/9	0/9
Artifactual Emphysema	4/9	2/9	0/9	0/9
Alveolar Duct Fibrosis	9/9	3/9	2/9	3/9
Thickening Bronchiolar Wall	0/9	0/9	1/9	2/9
Bronchiolar Epithelial Hyperplasia	0/9	2/9	1/9	1/9
Bronchiolar Epithelial Hypertrophy	0/9	0/9	2/9	1/9
Pneumonocyte Hyperplasia	1/9	2/9	0/9	2/9
Peribronchial Lymphoid Hyperplasia	1/9	1/9	0/9	0/9
Emphysema	0/9	2/9	0/9	0/9
Focal Necrosis	0/9	0/9	0/9	0/9
Focal Hemorrhage	0/9	0/9	0/9	0/9
Parasite	0/9	0/9	0/9	0/9
Perivascular Edema	0/9	0/9	0/9	0/9
Pulmonary Edema	0/9	0/9	0/9	0/9
Bronchiolitis	1/9	0/9	0/9	2/9
Bronchitis	0/9	0/9	1/9	0/9
Monkey Pox	0/9	0/9	0/9	0/9
Vasculitis	1/9	0/9	0/9	0/9
Granuloma	0/9	0/9	0/9	0/9
Pneumonitis	0/9	1/9	0/9	1/9
Abscess	0/9	0/9	0/9	0/9
Lung Mite Infestation	1/9	1/9	0/9	0/9
Adenomatosis	0/9	1/9	0/9	0/9
Bronchiectasis	0/9	3/9	0/9	0/9
Purulent Pneumonia	0/9	0/9	0/9	0/9
Epithelial Necrosis	0/9	0/9	0/9	0/9
Thickened Alveolar Wall	0/9	0/9	1/9	0/9
Pleuritis	0/9	0/9	0/9	0/9
Crystallin Material (yellow)	0/9	0/9	2/9	0/9
Mucous	0/9	0/9	0/9	0/9
Focal Fibrosis	0/9	0/9	0/9	0/9
Pleural Fibrosis	0/9	0/9	0/9	0/9
Alveolar Wall Fibrosis	0/9	0/9	2/9	2/9
Vacuolated Media	0/9	0/9	0/9	0/9
Endothelial hyperplasia	0/9	0/9	0/9	0/9
Stenotic	0/9	0/9	0/9	0/9
Chronic Pneumonia	0/9	0/9	0/9	0/9
Eroded Bronchi	0/9	0/9	0/9	0/9
Emphysematous Bulla	0/9	0/9	0/9	0/9

Table 39 - Continued

	GROUPS			
	<u>I</u>	<u>II</u>	<u>III</u>	<u>IV</u>
LUNG - Continued				
Atelectasis	0/9	0/9	0/9	0/9
Congested	0/9	0/9	0/9	0/9
Extravasated Blood	0/9	0/9	0/9	0/9
Collapsed Alveolar Wall	0/9	0/9	0/9	0/9
LIVER				
Pericholangitis	0/9	0/9	3/9	4/9
Bile Duct Proliferation	1/9	2/9	3/9	3/9
Focal Necrosis	0/9	0/9	0/9	0/9
Sinusoidal Pigment	2/9	9/9	2/9	2/9
Focal Hepatitis	0/9	0/9	0/9	0/9
Focal Lymphoid Infiltration	1/9	1/9	1/9	0/9
Nematodiasis	0/9	0/9	0/9	0/9
Thick Capsule	0/9	0/9	0/9	0/9
Granuloma	0/9	0/9	0/9	0/9
Abscess	0/9	0/9	0/9	0/9
Hepatocyte Vacuolation	0/9	1/9	1/9	2/9
Greenish Granular Material in the Hepatocytes	0/9	0/9	1/9	0/9
PERIBRONCHIAL LYMPH NODE				
Phagocytized Pigment	6/9	7/9	7/9	8/9
Lymphoid Activity	8/9	4/9	0/9	0/9
Lymphoid Atrophy	0/9	0/9	0/9	0/9
Adenitis	0/9	0/9	0/9	0/9
Granuloma	1/9	0/9	0/9	0/9
Reticuloendothelial Cell Hyperplasia	1/9	1/9	0/9	0/9
Lymphadenitis	0/9	0/9	0/9	0/9
TRACHEA				
Tracheitis	1/9	1/9	0/9	0/9
Increase in Goblet Cells	0/9	1/9	0/9	0/9
Exudate in Lumen	0/9	0/9	0/9	0/9
Necrosis of the Epithelium	0/9	0/9	0/9	0/9
Inclusion Bodies	0/9	0/9	0/9	0/9
Epithelial Hyperplasia	0/9	0/9	0/9	0/9
Cilia Atrophy	0/9	1/9	0/9	0/9
Squamous Metaplasia	0/9	1/9	0/9	0/9
Focal Hemorrhage	0/9	0/9	0/9	0/9

Table 39 - Continued

	GROUPS			
	<u>I</u>	<u>II</u>	<u>III</u>	<u>IV</u>
KIDNEY				
Interstitial Nephritis	0/9	1/9	2/9	2/9
Epithelial Vacuolation	1/9	0/9	3/9	7/9
Tubular Dilatation	3/9	1/9	0/9	1/9
Loss of the Brush Border	0/9	0/9	3/9	5/9
Nuclear Vesiculation	0/9	0/9	0/9	4/9
Tubular Hypertrophy	0/9	0/9	0/9	3/9
Pyelitis	0/9	1/9	0/9	0/9
Focal Mineralization	0/9	0/9	1/9	0/9
Glomerular Degeneration	0/9	0/9	0/9	0/9
Inclusion Bodies	0/9	0/9	7/9	9/9
Vasculitis	0/9	0/9	0/9	0/9
Congestion	0/9	0/9	0/9	1/9
Focal Fibrosis	0/9	0/9	0/9	1/9
Perirenal Abscess	0/9	0/9	0/9	0/9
Protein Inhibition	0/9	0/9	1/9	6/9
Intima Thickening	0/9	0/9	0/9	0/9
Endothelial Hyperplasia	0/9	0/9	0/9	0/9
HEART				
Focal Myocarditis	3/9	2/9	0/9	2/9
Endocarditis	0/9	0/9	0/9	0/9
Epicarditis	0/9	0/9	0/9	0/9
Myocardial Degeneration	1/9	0/9	0/9	0/9
Vasculitis	0/9	0/9	0/9	0/9
Subendocardial Hemorrhage	0/9	0/9	0/9	0/9
Thickened Endocardium	0/9	0/9	0/9	0/9
Focal Hyperplasia in the Endothelium	0/9	0/9	0/9	0/9
Intima Thickening	0/9	0/9	0/9	0/9
Granular Pigment	0/9	0/9	0/9	0/9



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V. STATISTICAL GROUPING C - RESULTS OF THE CHRONIC EXPOSURE OF CYNOMOLGUS MONKEYS TO 9.70 PPM SULFUR DIOXIDE (SO₂), 0.51 MG/M³ LEAD CHLOROBROMIDE (PbClBr), AND 9.93 PPM SO₂ COMBINED WITH 0.50 MG/M³ PbClBr.

Four groups of animals comprise the third statistical grouping-C. One group was maintained as the control group exposed to filtered room air, while the other three groups were exposed to sulfur dioxide and lead chlorobromide singly and in binary combination. Group designations used throughout this section are presented in Table 12.

Table 12 - Group C designations

<u>Group Designation (No.)</u>	<u>Agent</u>	<u>Nominal Concentration</u>	<u>Mean Analytical Concentration</u>
I (1)	Control	0	0
II (5)	SO ₂	10.00 ppm	9.70 ppm
III (9)	PbClBr	0.60 mg/m ³	0.51 mg/m ³
IV (18)	SO ₂	10.00 ppm	9.93 ppm
	PbClBr	0.60 mg/m ³	0.50 mg/m ³

1. Exposure concentrations

The chamber concentrations as determined analytically are presented in Tables 1, 2, and 3, Appendix C for Groups II, III, and IV, respectively. The mean and standard deviation for the group exposed to SO₂ alone was 9.70 ppm ± 1.10; for the group exposed to PbClBr alone 0.51 mg/m³ ± 0.27; and for the group exposed to the combination of SO₂ and PbClBr, the means and standard deviations were 9.93 ppm ± 1.03 and 0.50 mg/m³ ± 0.27, respectively.



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2. Particle Size Determination

The mean and geometric deviation of all count particle size determinations for PbClBr converted to mass median diameter (MMD) were $0.550\mu \pm 1.57$ and $1.130\mu \pm 1.84$ for Groups III and IV, respectively. A composite size vs. distribution log-probability plot from the pooled count data is presented in Figures 50 and 51 for Groups III and IV, respectively.

3. Biological Measurements

3.1. Body Weight

Analysis of variance of regression (Table 4, Appendix C) indicated significant slopes among the groups. No significant differences in growth rate were found between Group I and the other groups. Figure 52 presents the linear regression curves for the four groups.

3.2. Survival

No deaths occurred in Groups I, III, or IV during the 104-week exposure period. One monkey in Group II was sacrificed in Week 40 due to extensive monkey pox lesions. Daily observation of the animals revealed no clinical signs of toxicity or abnormal behavior attributable to the exposure atmosphere.

3.3. Pulmonary Function Tests

3.3.1. Mechanical Properties of the Lung and Respiratory System

3.3.1.1. Total Respiratory System Flow Resistance During Inspiration [Rrs(i)]

Analysis of variance of regression for Rrs(i) (Table 5, Appendix C) revealed non-parallelism among the groups. The third degree polynomial regression

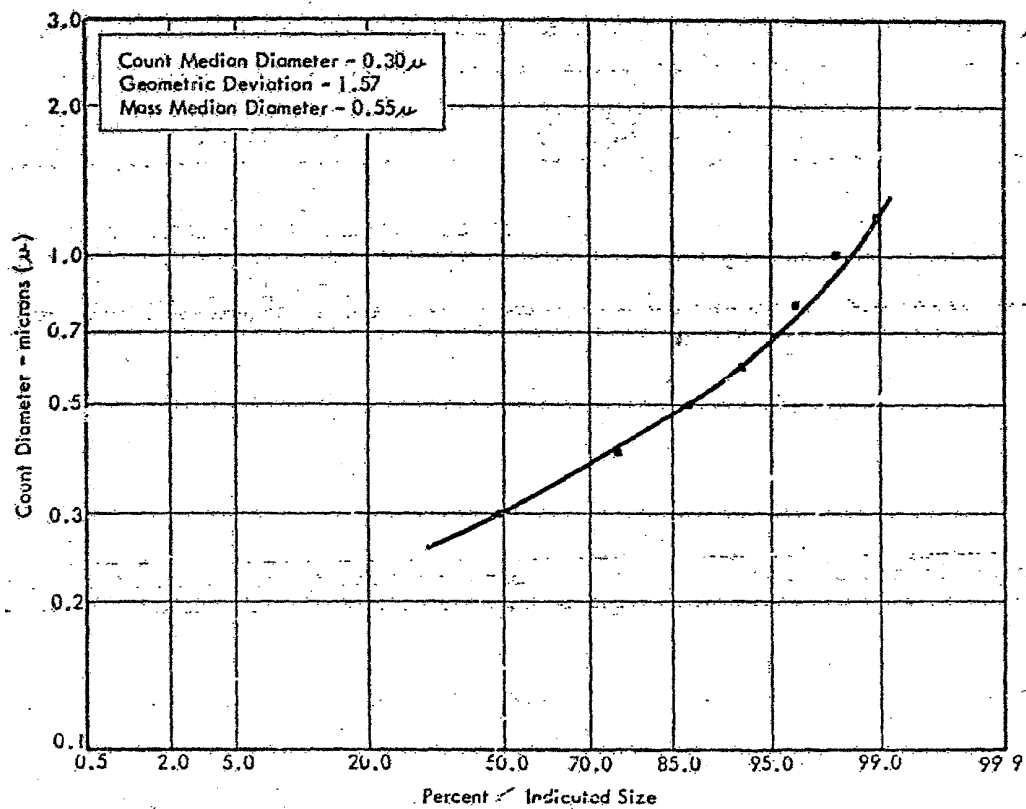


Figure 50 -- Particle size distributions (count diameter) of PbClBr.

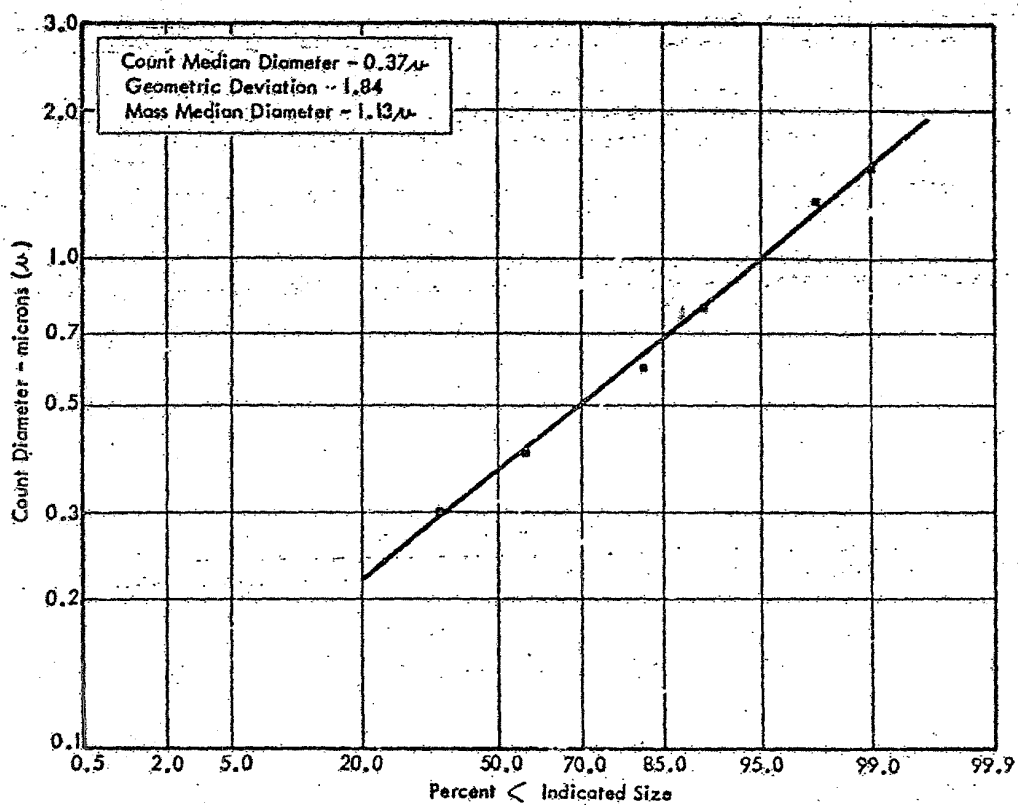


Figure 51 - Particle size distributions (count diameter) of PbClBr for the group exposed to the combination of PbClBr and SO₂.

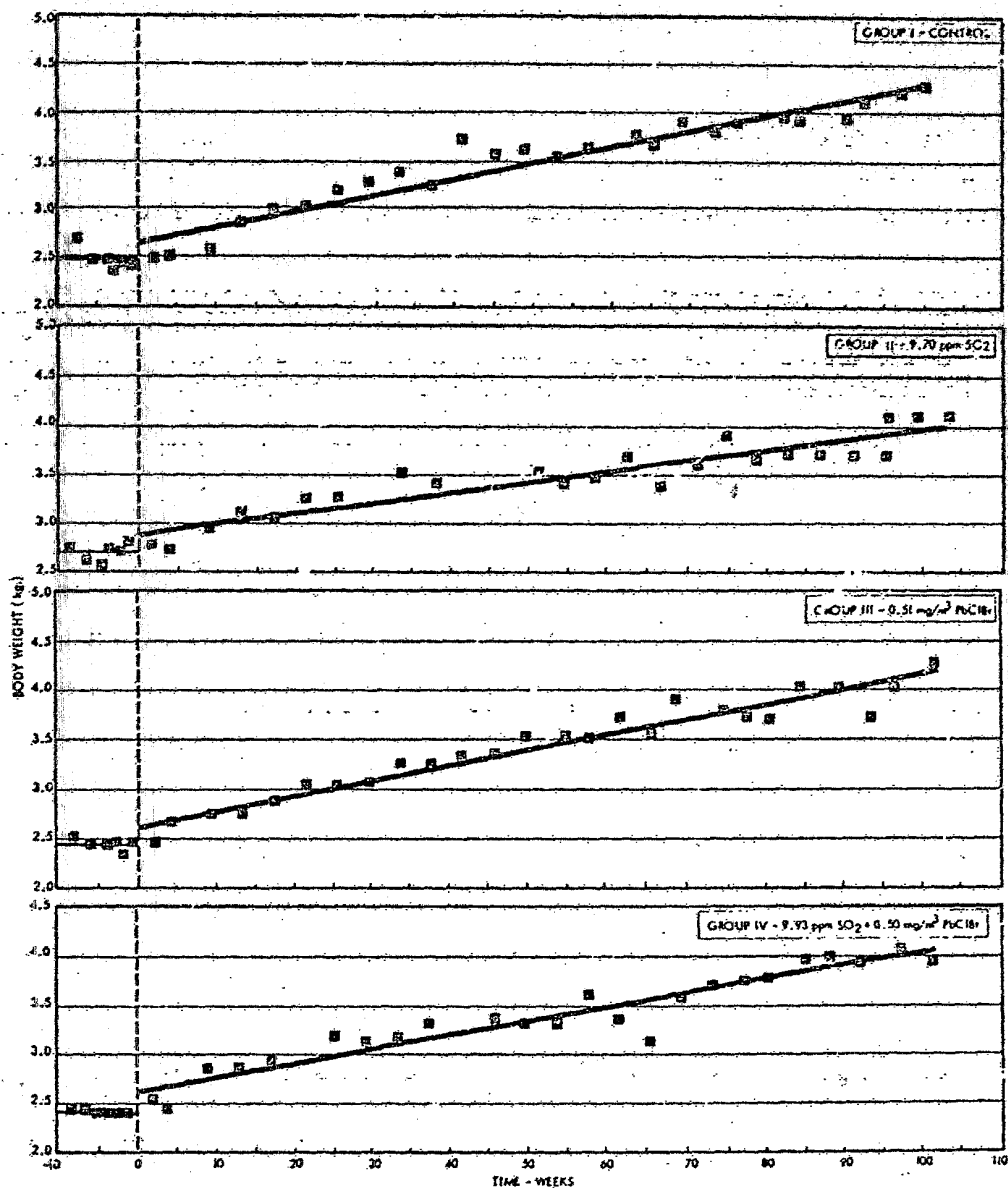


Figure 52 - First degree polynomial regression curves for body weight prior to and during exposure to sulfur dioxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.



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curves (Figure 54) indicated that $Rrs(i)$ values for Group III were slightly higher than Group I during the first nine weeks of exposure, but thereafter were similar to Group I. A t-test of the pre-exposure adjusted means for this early interval was significant ($t = 4.33$, d.f. = 16). A similar test comparing Group IV with Group I also yielded a significant t value ($t = 2.39$, d.f. = 16).

3.3.1.2. Total Respiratory System Flow Resistance During Expiration [$Rrs(e)$]

Analysis of variance of regression for $Rrs(e)$ (Table 6, Appendix C) indicated non-parallelism among the groups. The third degree polynomial regression curves (Figure 54) indicated that Group I decreased with time slightly more than the other groups, starting from higher pre-exposure values. A t-test of pre-exposure adjusted overall exposure means indicated that Group IV was significantly higher throughout ($t = 3.63$, d.f. = 16) and indicated a significant difference between Groups I and II ($t = 2.89$, d.f. = 16). Group III was not significantly different from Group I by this test ($t = 1.92$, d.f. = 16).

3.3.1.3. Tidal Volume (V_T)

Analysis of variance of regression for V_T (Table 7, Appendix C) revealed no significant slope differences among the groups. The third degree polynomial regression curves (Figure 55) indicated that all groups increased with time.

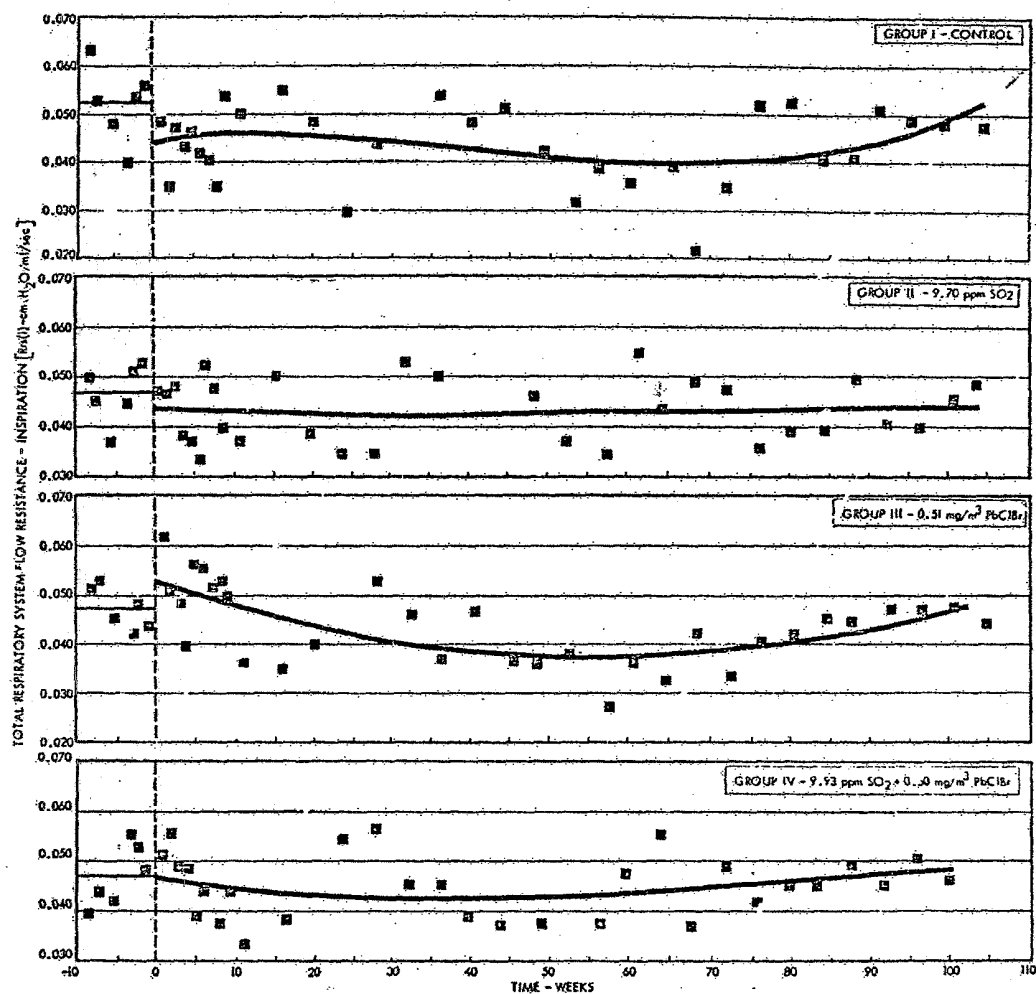


Figure 53 - Third degree polynomial regression curves for $P_{rs}(i)$ prior to and during exposure to sulfur dioxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.

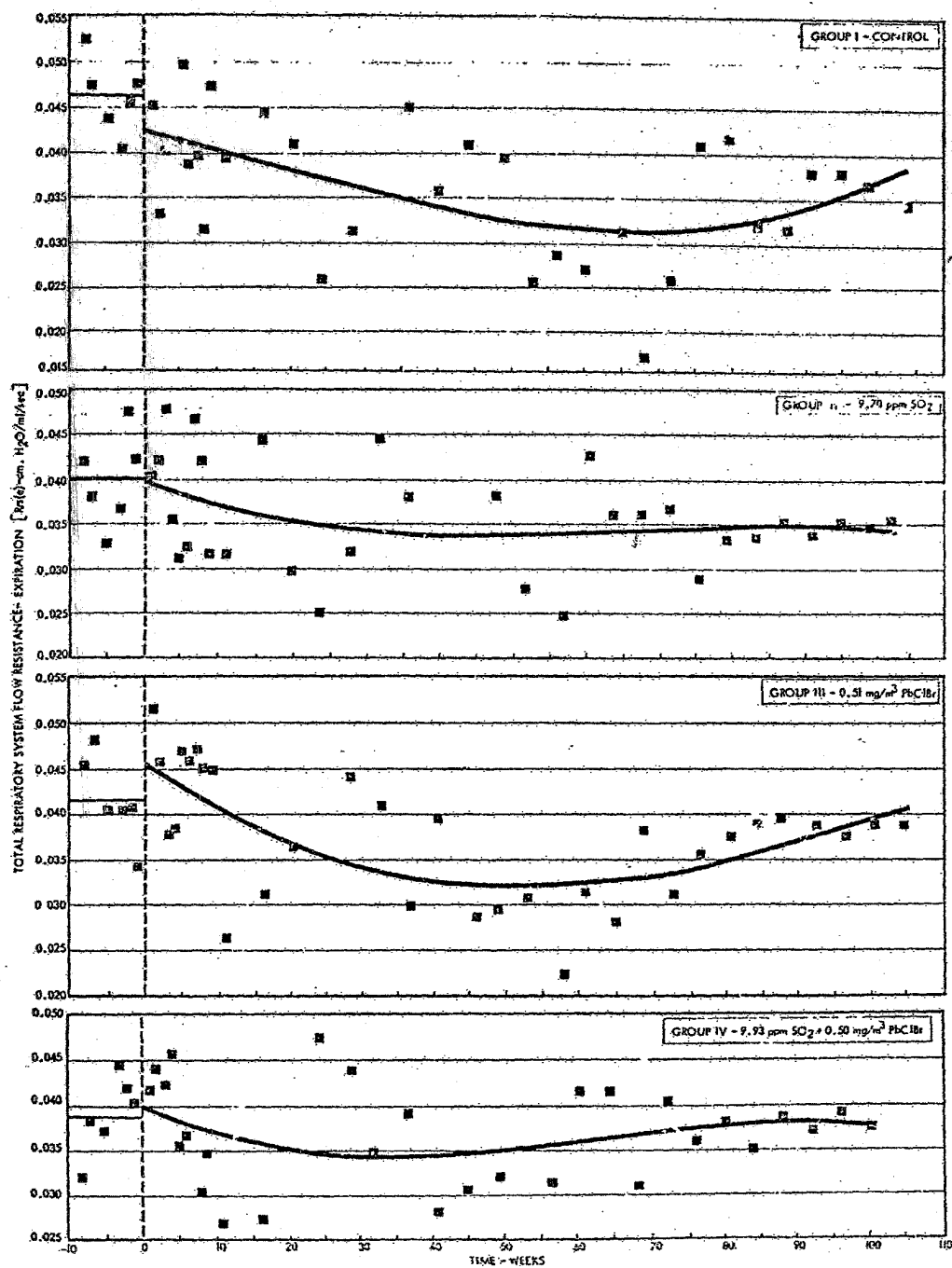


Figure 54- Third degree polynomial regression curves for $R_{rs}(e)$ prior to and during exposure to sulfur dioxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.

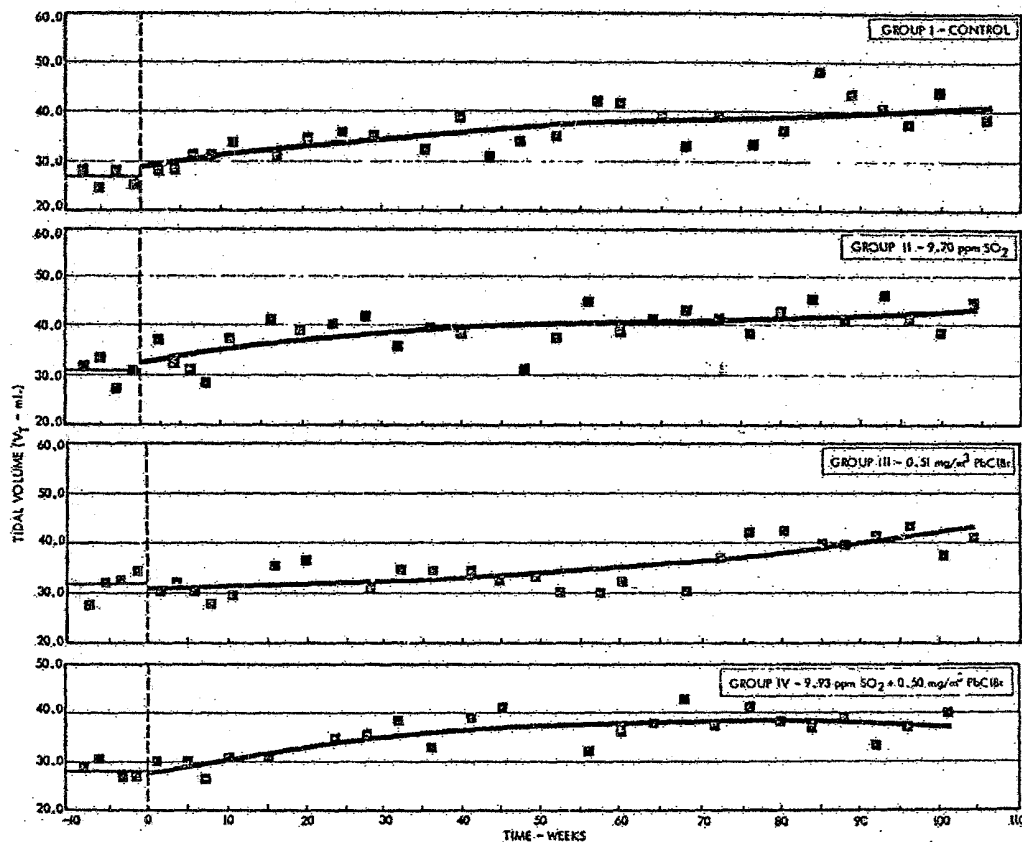


Figure 55 - Third degree polynomial regression curves for V_T prior to and during exposure to sulfur dioxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.



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3.3.1.4. Respiratory Rate (RR)

Analysis of variance of regression for RR (Table 8, Appendix C) indicated non-parallelism among the groups. The third degree polynomial regression curves are shown in Figure 56. Inspection of Figure 56 indicated that RR values for Group IV were slightly higher during the pre-exposure period and remained slightly higher throughout the exposure period.

3.3.1.5. Dynamic compliance of the Lung [Cdyn(1)]

Analysis of variance of regression for Cdyn(1) (Table 9, Appendix C) revealed non-parallelism among the groups. The third degree polynomial regression curves are shown in Figure 57. Inspection of Figure 57 shows that Group I, which was considerably lower in Cdyn(1) during the pre-exposure period, had a marked increase at the start of the "exposure" period and increased slightly thereafter as did Groups III and IV. Group II, on the other hand, started from a higher pre-exposure level, increased at the start of exposure but did not increase further. The difference between the pre-exposure adjusted overall means of Groups I and II was not significant ($t = 1.87$, d.f. = 15). The pre-exposure adjusted differences in the means of the first year for Group I vs. Group III and for Group I vs. Group IV were significant ($t = 2.69$, d.f. = 16 and $t = 2.30$, d.f. = 16, respectively); however, the large jump between the pre-exposure values and the start of the "exposure" period in Group I renders difficult any interpretation of these differences.

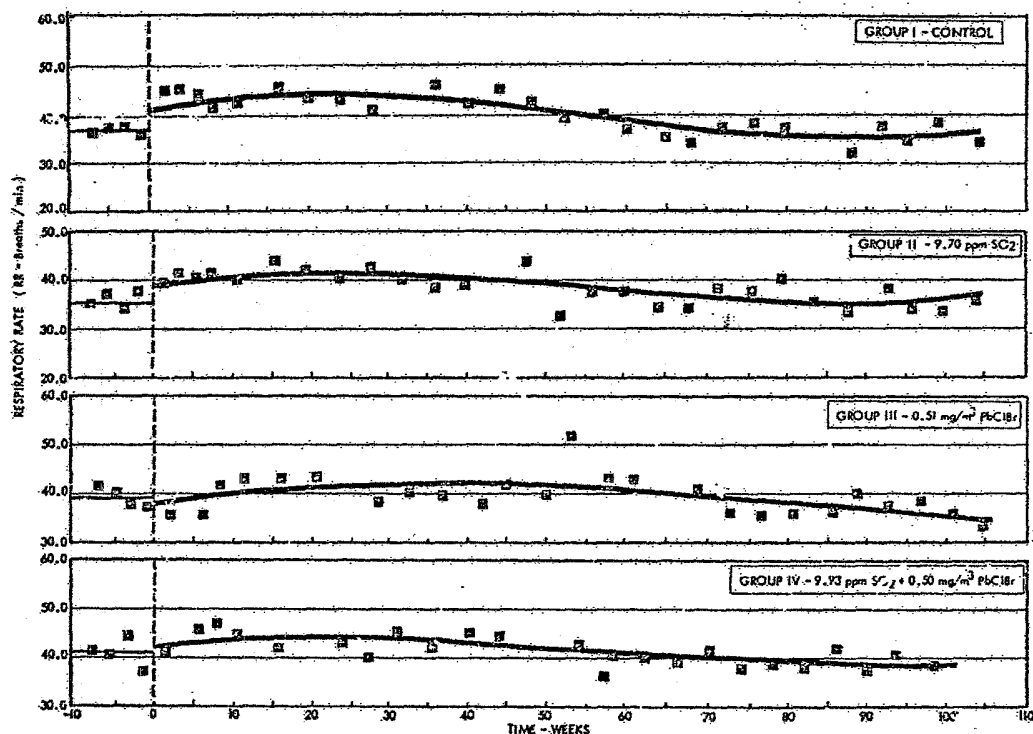


Figure 56 - Third degree polynomial regression curves for RR prior to and during exposure to sulfur dioxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.

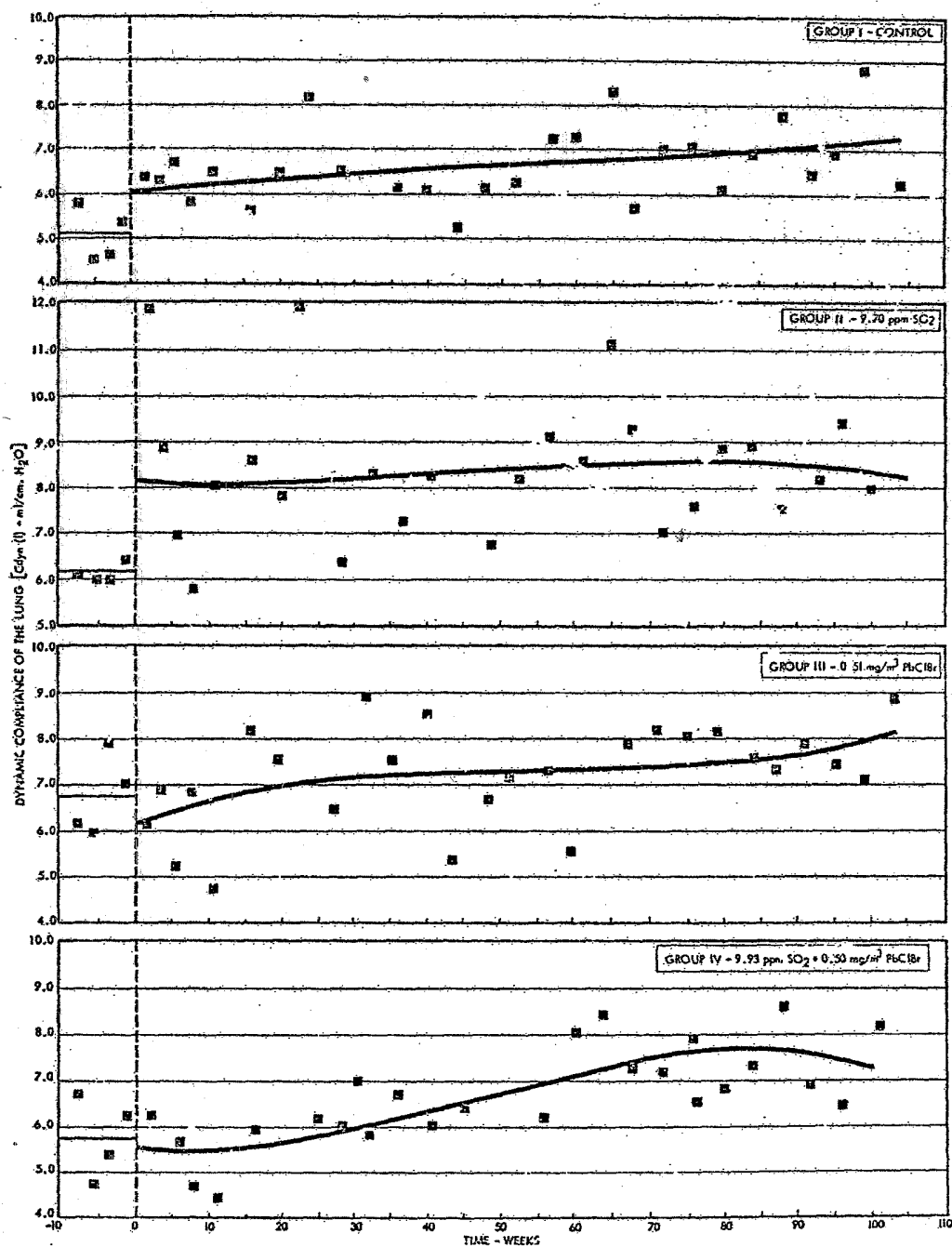


Figure 57 - Third degree polynomial regression curves for $C_{dyn}(l)$ prior to and during exposure to sulfur dioxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.



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3.3.1.6. Pulmonary Flow Resistance (R_I)

Analysis of variance of regression for R_I (Table 10, Appendix C) indicated non-parallelism among the groups. The third degree polynomial regression curves are presented in Figure 58. Inspection of this Figure indicates that the trends with time differed among the groups, but that the R_I values were generally similar for all groups, except Group I, which did not decrease as much with time. A t-test of the pre-exposure adjusted means of the first nine weeks of exposure indicated that Group IV was significantly higher than Group I ($t = 2.39$, d.f. = 16) as was Group III ($t = 2.66$, d.f. = 16).

3.3.1.7. Work of Breathing During Inspiration per ml Tidal Volume [$W(i)/ml V_T$]

Analysis of variance of regression for $W(i)/ml V_T$ (Table 11, Appendix C) revealed non-parallelism among the groups. The third degree polynomial regression curves are presented in Figure 59. Inspection of this Figure indicates that both Groups III and IV had lower values than Group I throughout the study.

3.3.1.8. Work of Breathing During Expiration per ml Tidal Volume [$W(e)/ml V_T$]

Analysis of variance of regression for $W(e)/ml V_T$ (Table 12, Appendix C) indicated no significant slope differences among the groups. The third degree polynomial regression curves (Figure 60) also indicated no observable differences among the groups.

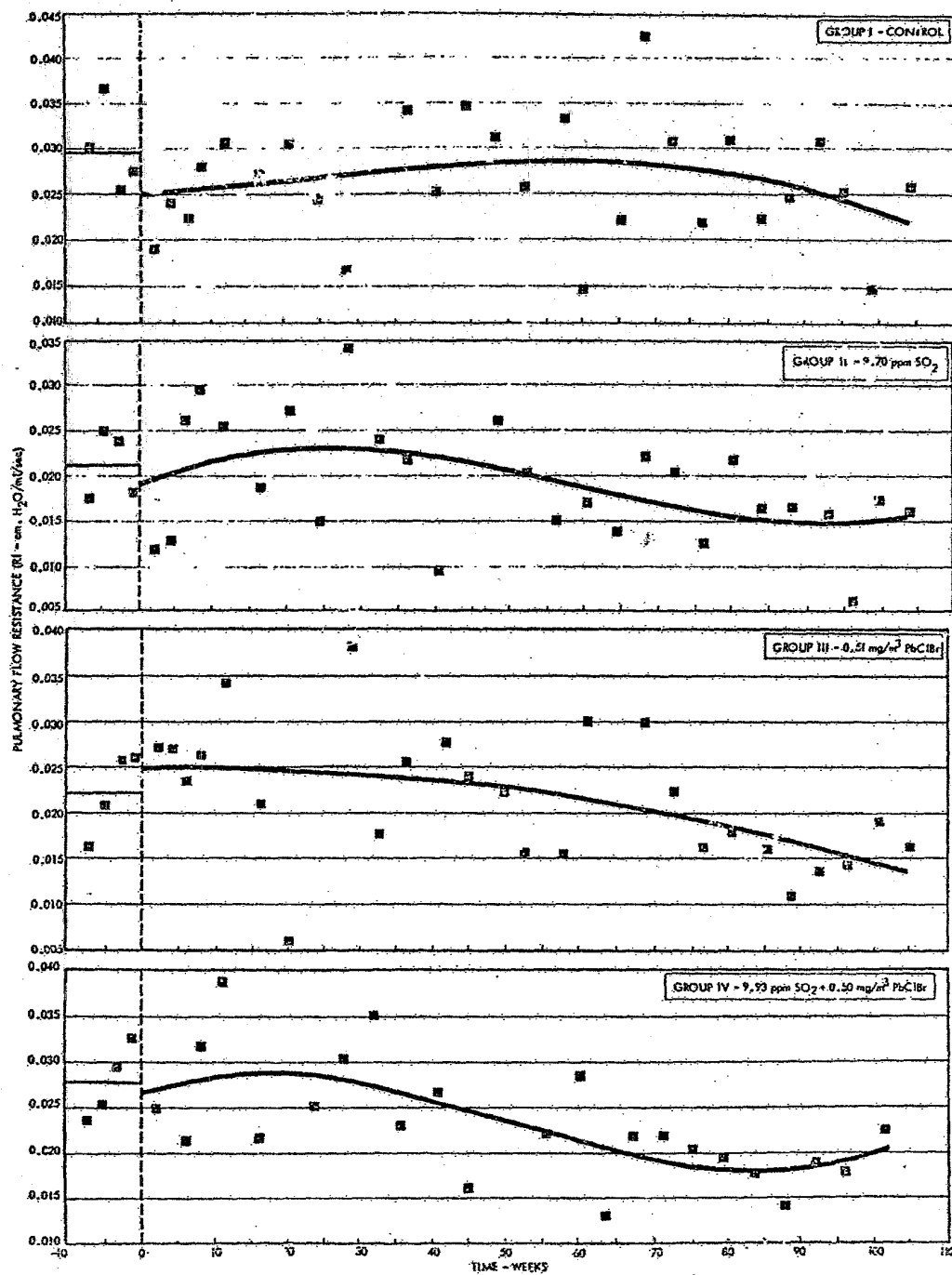


Figure 58 - Third degree polynomial regression curves for Rl prior to and during exposure to sulfur dioxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.

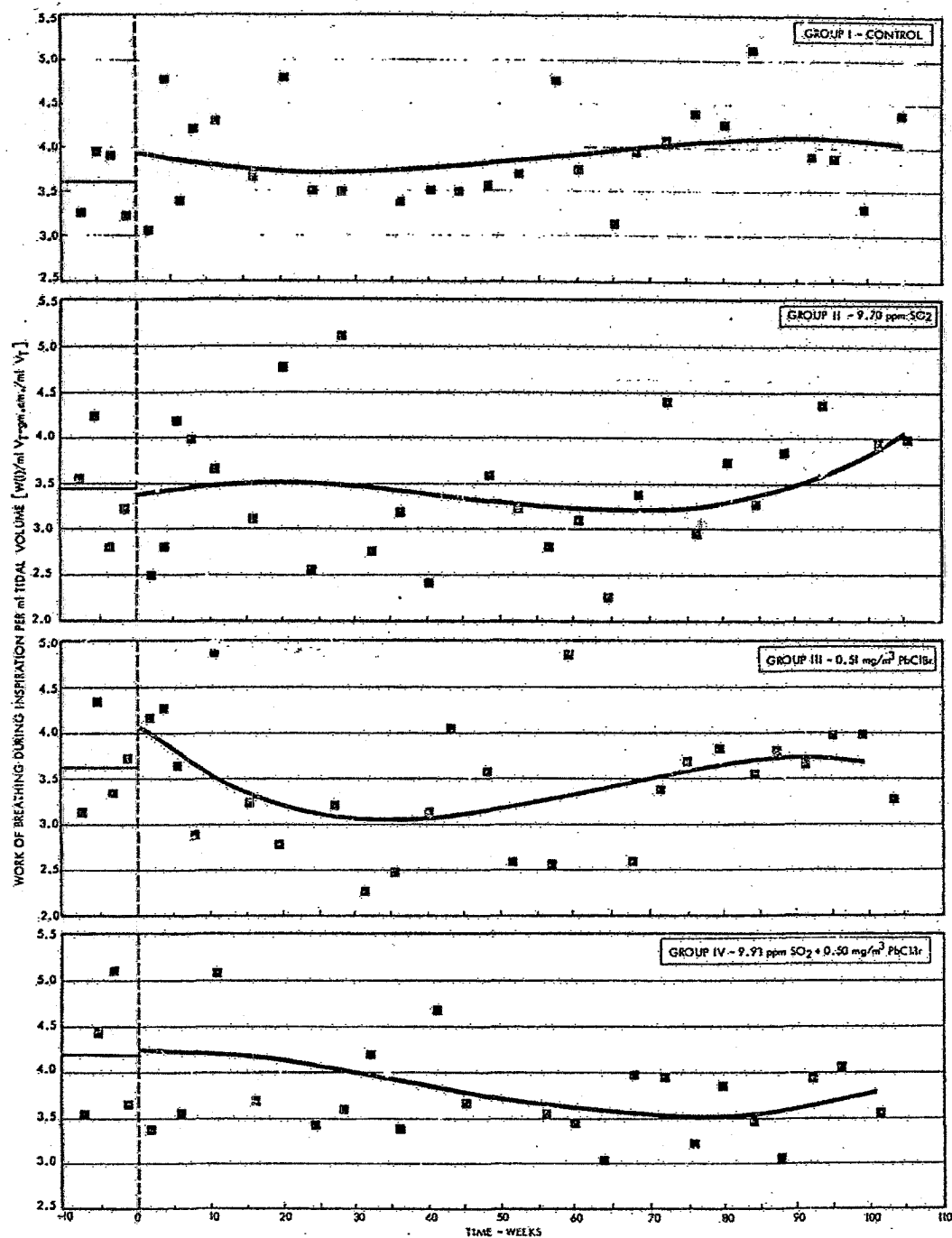


Figure 59 - Third degree polynomial regression curves for $W(i)/ml V_T$ prior to and during exposure to sulfur dioxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.

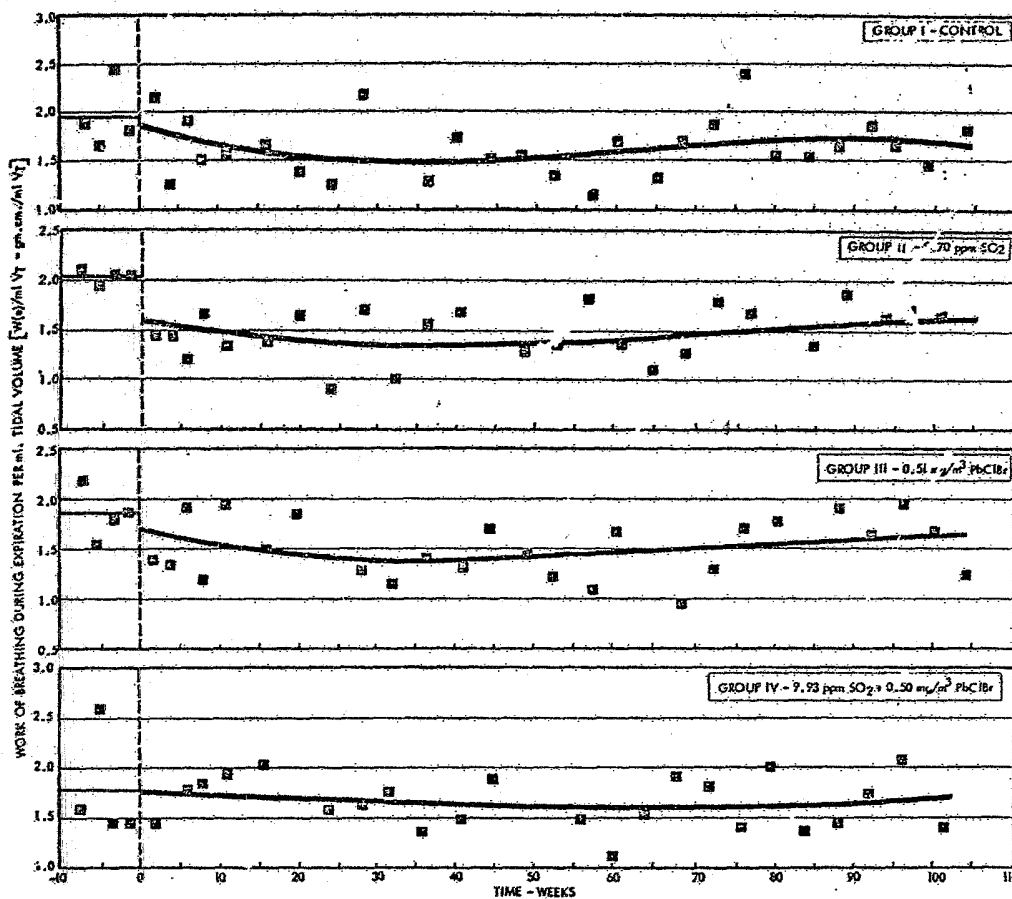


Figure 60 - Third degree polynomial regression curves for $W(e)/ml V_T$ prior to and during exposure to sulfur dioxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.



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3.3.2. Diffusion

3.3.2.1. Diffusing Capacity of the Lung for Carbon Monoxide (DL_{CO})

Analysis of variance of regression for DL_{CO} (Table 13, Appendix C) revealed no significant slope differences among the groups. The third degree polynomial regression curves (Figure 61) indicated that DL_{CO} for all groups increased with time.

3.3.3. Distribution of Inspired Air, Nitrogen Washout

3.3.3.1. Number of Breaths from 80% to 1% Nitrogen [$N(1\% N_2)$]

Analysis of variance of regression for $N(1\% N_2)$ (Table 14, Appendix C) indicated no significant slope differences among the groups. Inspection of the third degree polynomial regression curves (Figure 62), indicated that $N(1\% N_2)$ values for Group I were somewhat higher during the pre-exposure control period than values for Groups II, III, and IV. During the entire exposure period, $N(1\% N_2)$ values for Groups I and II were similar, but values for Groups III and IV were at a higher level. Separate t-tests of the pre-exposure adjusted overall exposure means were made to compare Group I with Groups II, III, and IV during the exposure period. These tests indicated that Groups II, III, and IV were each significantly higher than Group I ($t = 2.77$, d.f. = 16; $t = 4.55$, d.f. = 16; and $t = 3.26$, d.f. = 16, respectively).

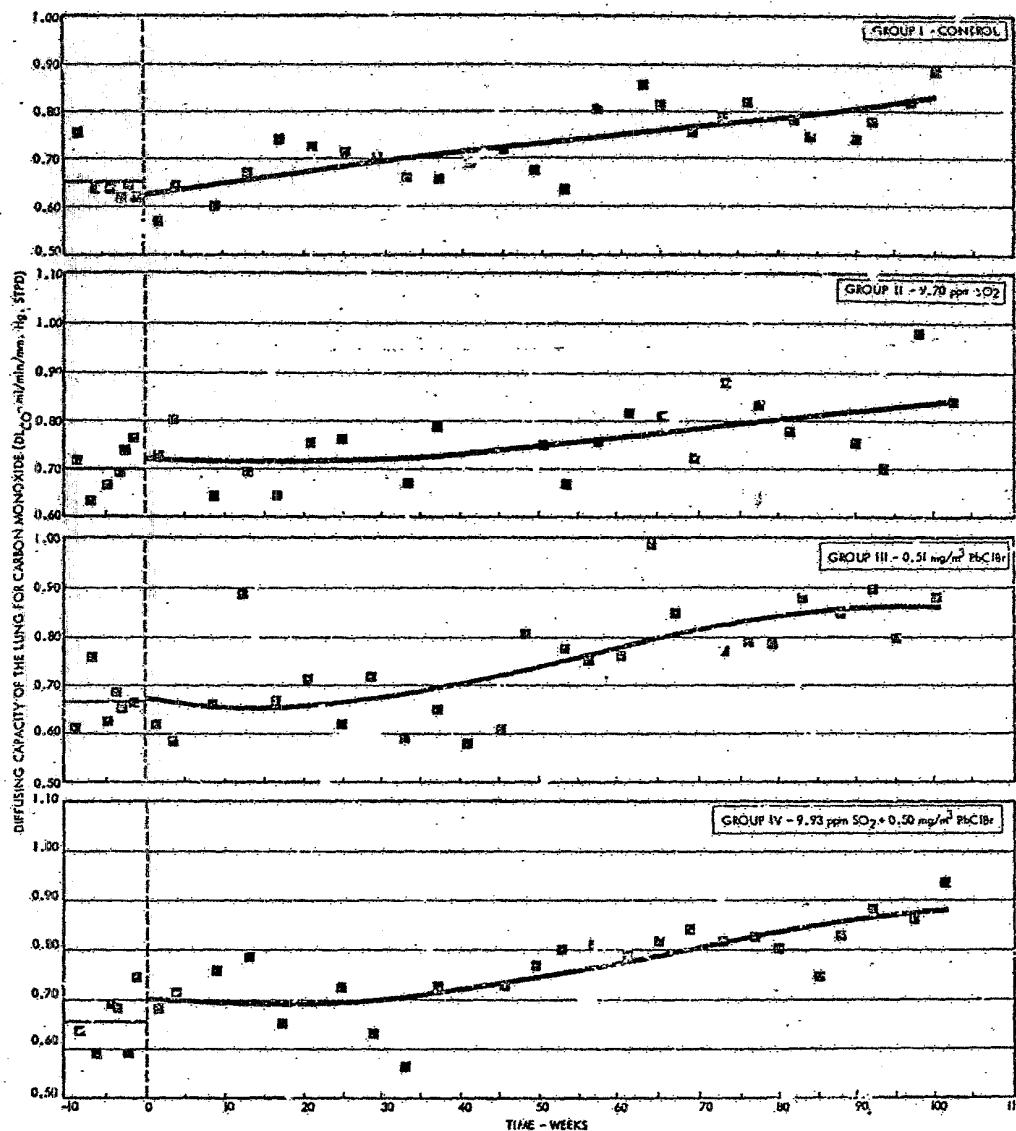


Figure 61 - Third degree polynomial regression curves for DLCO prior to and during exposure to sulfur dioxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.

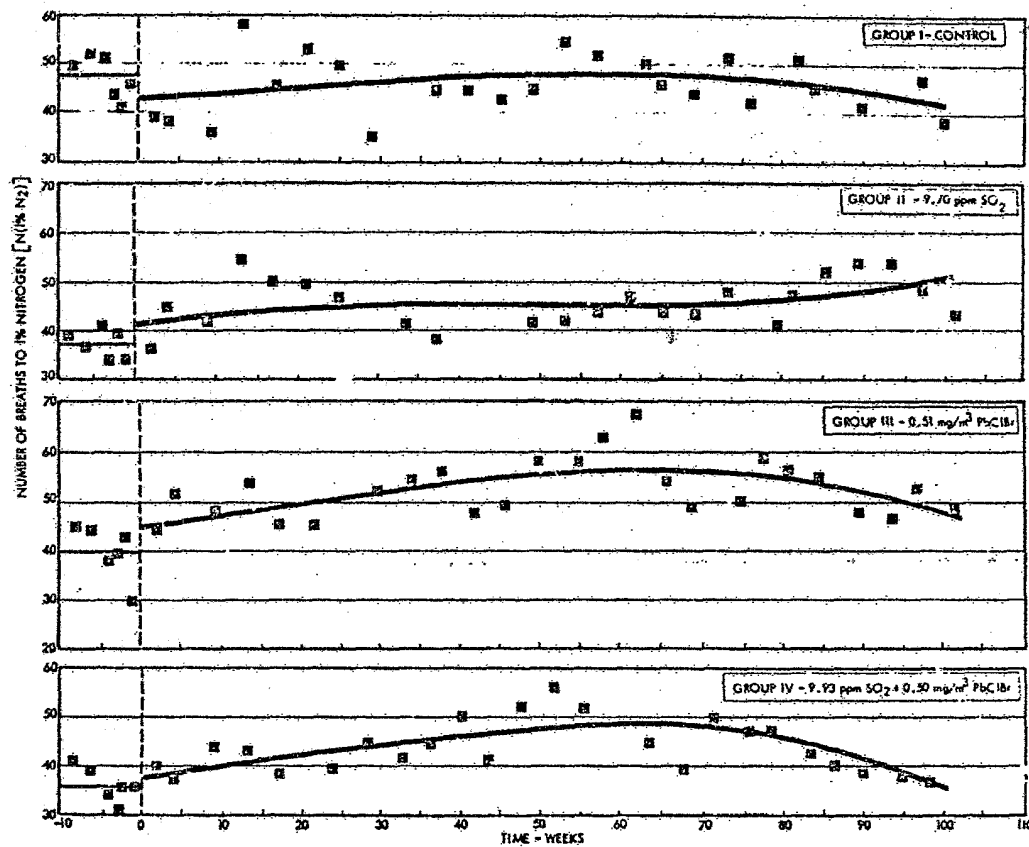


Figure 62 - Third degree polynomial regression curves for N(1% N₂) prior to and during exposure to sulfur dioxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.



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3.3.3.2. Respiratory Rate Measured During Pure Oxygen Breathing (RR')

Analysis of variance of regression for RR' (Table 15, Appendix C) indicated no significant slope differences among the groups. The third degree polynomial regression curves are presented in Figure 63. Inspection of Figure 63 indicated that RR' values for Groups I and II were essentially the same during the pre-exposure period and the entire exposure period. However, RR' values for Groups III and IV were higher than Group I following the forty-fifth week of exposure, and remained higher until the end of the experiment. Separate t-tests of the pre-exposure adjusted overall exposure means indicated that both Groups III and IV were significantly higher than Group I ($t = 2.61$, d.f. = 16 and $t = 2.28$, d.f. = 16, respectively).

3.3.3.3. Cumulative Tidal Volume from 80% to 1% Nitrogen [$CV_T(1\% N_2)$]

Analysis of variance of regression for $CV_T(1\% N_2)$ (Table 16, Appendix C) indicated no significant slope differences among the groups. The third degree polynomial regression curves are presented in Figure 64. Inspection of Figure 64 indicated that Group IV had somewhat lower CV_T values during the pre-exposure period and generally remained lower than the CV_T values for the other three groups during the exposure period. Values for Group III were slightly higher overall than Group I throughout the exposure period. A t-test of the pre-exposure adjusted overall exposure means comparing Groups I and III indicated that Group III was significantly higher ($t = 2.24$, d.f. = 13.7) throughout the exposure period.

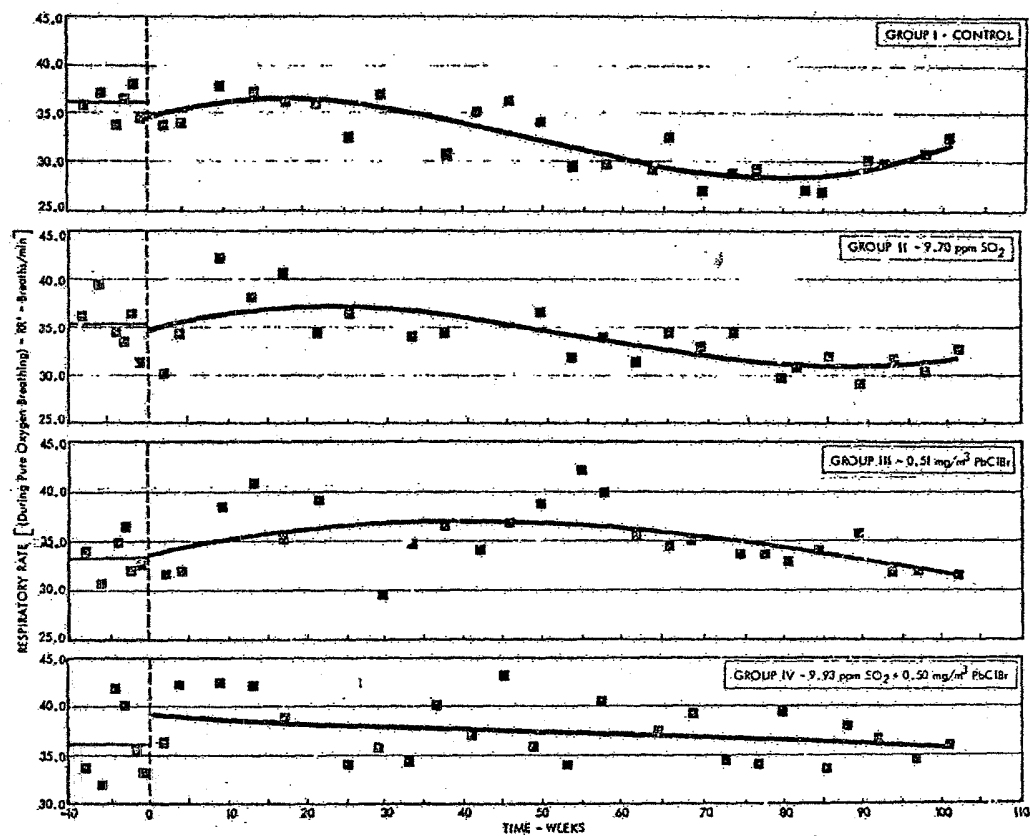


Figure 63 - Third degree polynomial regression curves for RR' prior to and during exposure to sulfur dioxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.

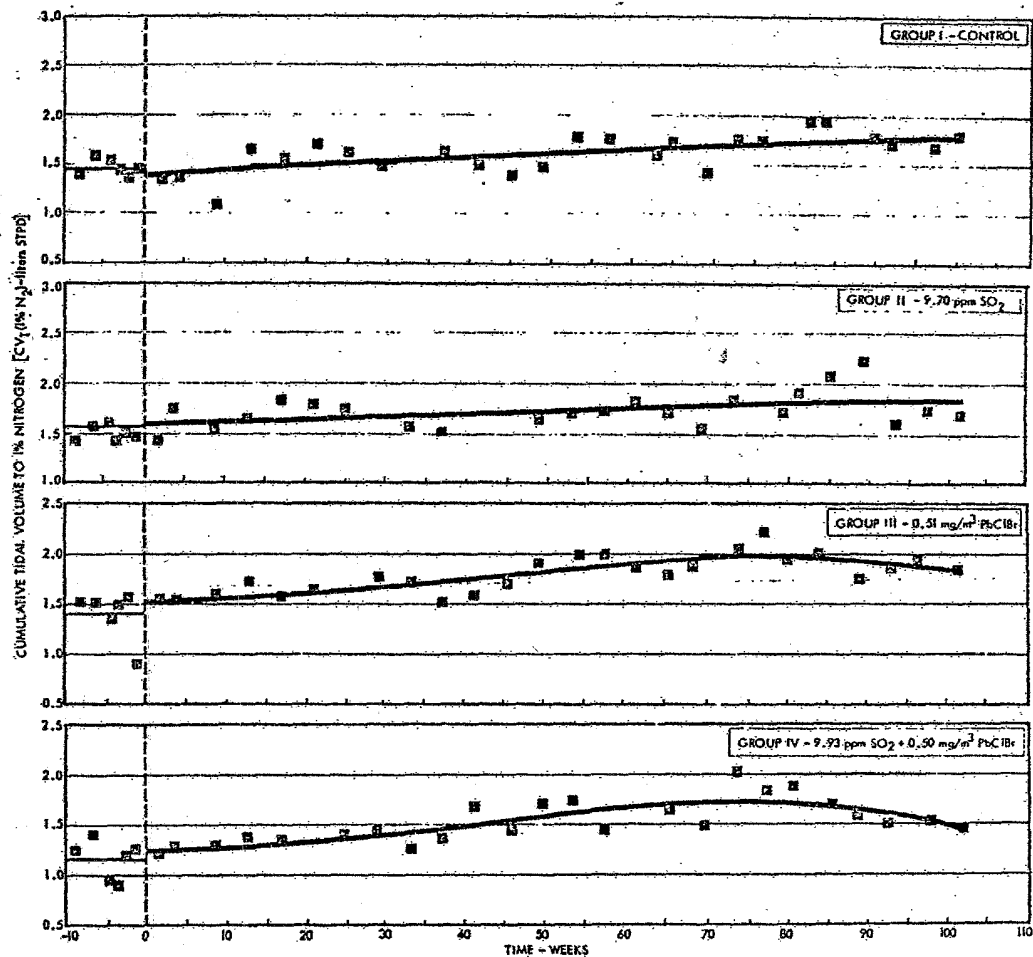


Figure 64 - Third degree polynomial regression curves for CVT(1% N₂) prior to and during exposure to sulfur dioxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.



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3.3.3.4. Tidal Volume Measured During Pure Oxygen Breathing (V_T')

Analysis of variance of regression for V_T' (Table 17, Appendix C) revealed non-parallelism among the groups. The third degree polynomial regression curves are presented in Figure 65. Inspection of Figure 65 indicated that Groups I, III, and IV increased slightly with time while Group II maintained a constant level throughout the experiment. A t-test of the pre-exposure adjusted overall exposure means indicated that Group II was significantly lower than Group I ($t = 2.44$, d.f. = 16) throughout the exposure period.

3.4. Hematology

The group means and analysis of variances of the various hematological variables measured are presented in Tables 18, 19, 20, and 21, Appendix C. No consistent trends were noted in any of these variables which remained within normal limits throughout. Random statistically significant differences were seen, but were not consistently related to the exposure conditions.

3.5. Clinical Biochemistry

The group means, standard errors, and the results of the analysis of variance of the various clinical biochemical variables measured are presented in Tables 22 through 35, Appendix C. Scattered statistically significant differences were noted; however, no trends were seen in any of the variables. Throughout the study, the group mean values fluctuated within the normal ranges of these variables.

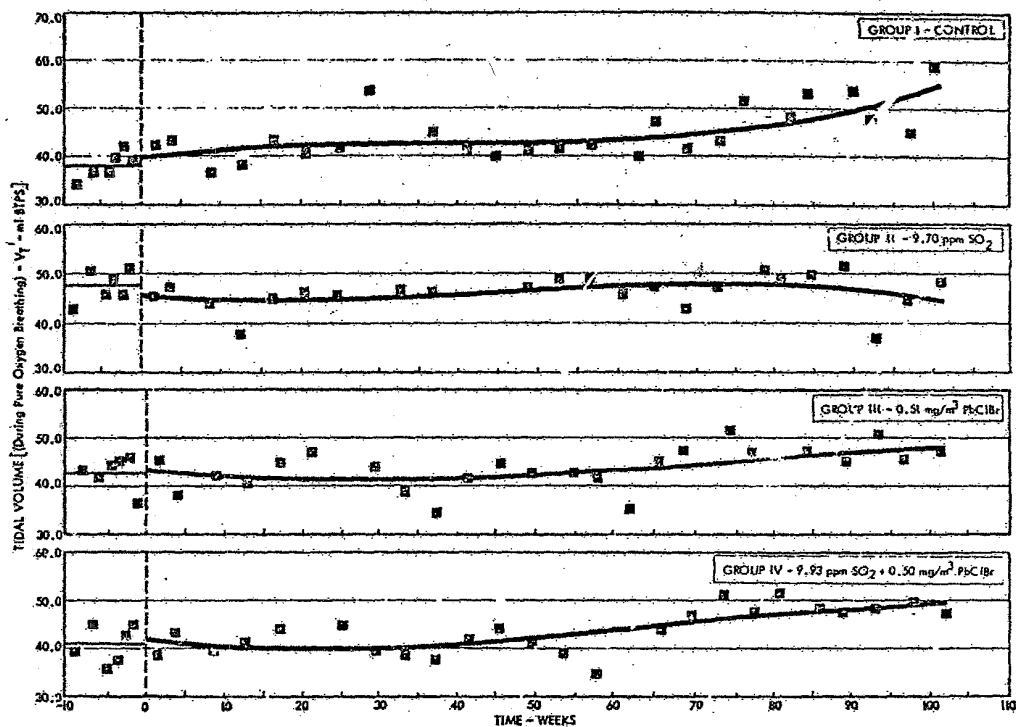


Figure 65 - Third degree polynomial regression curves for V_T prior to and during exposure to sulfur dioxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.



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3.6. Arterial Blood Gas and pH

The group means and standard errors for the blood gas variables are presented in Table 36, Appendix C. Examination of these data did not reveal any consistent trend with time. No apparent exposure-related changes were seen in any of these variables.

3.7. Terminal Body Weight, Organ Weight, and Organ Weight as a Percentage of Body Weight

The data of the terminal body weight, organ weight, and organ/body weight ratios are presented in Tables 37 and 38, Appendix C for males and females, respectively. Several significant differences were found between the experimental groups and the control group. The adrenal weight for the males in Group II was significantly higher than Group I, and the adrenal weight and adrenal weight/body weight ratios for Group IV males were higher than Group I. The liver weight/body weight ratio for Group IV females was significantly higher than for Group I females. Several other significant differences were found from comparisons made between the various experimental groups; however, no consistent trends could be discerned.

3.8. Histopathology Summary

A detailed listing of the microscopic alterations seen in the lungs, tracheas, livers, kidneys, peribronchial lymph nodes, and hearts from the animals in the control and exposure groups are found in Table 39, Appendix C. Microscopic examination of the tissues from the animals exposed to $0.6 \text{ mg/m}^3 \text{ PbClBr}$ and to the combination of $0.6 \text{ mg/m}^3 \text{ PbClBr}$ and 10.0 ppm SO_2 revealed exposure-related alterations in the kidneys. These microscopic alterations were characterized by varying degrees of degeneration in the



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proximal convoluted tubules. The epithelial cells of the proximal convoluted tubules were vacuolated and possessed vesiculated nuclei. Numerous intranuclear, acid fast inclusion bodies were seen in the epithelial cells of the proximal convoluted tubules.

No other exposure-related microscopic alterations were seen in the lungs, liver, trachea, peribronchial lymph node or hearts. Scattered incidental lesions were seen in these organs from both the control and test animals. No difference in the incidence and severity of these lesions was seen when the controls were compared with the exposed groups.

Animal number 182L in the group exposed to 10.0 ppm SO_2 died during the 40th week of exposure. Microscopic examination of the tissues from this animal revealed lesions consistent of monkey pox in the lungs, liver, and trachea.

3.9. Summary

The inhalation exposure of male and female cynomolgus monkeys to 9.70 ppm SO_2 , 0.51 mg/m^3 PbClBr , and the combination of 9.93 ppm SO_2 plus 0.50 mg/m^3 PbClBr resulted in a deterioration in the distribution of ventilation in the animals in the two groups containing PbClBr . The number of breaths to 1% nitrogen and respiratory rate measured during pure oxygen breathing for both groups were significantly elevated above the controls, with respect to their relative pre-exposure values throughout the exposure period. Cumulative tidal volume to 1% nitrogen was significantly elevated in the group exposed to PbClBr alone, but this change was not seen in the



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group exposed to the combination of SO_2 and PbClBr . With the exception of higher breath to 1% nitrogen values than the control group, none of these differences were observed in the group exposed to 9.70 ppm SO_2 . This one difference was probably due to the high pre-exposure values of the control group.

Microscopic alterations related to the exposure to PbClBr were found in the kidneys of the animals of these two groups. These histopathological changes were characterized by varying degrees of degeneration of the proximal convoluted tubules. The epithelial cells of these tubules were vacuolated and possessed vesiculated nuclei. Numerous intranuclear, acid fast inclusion bodies were seen in these epithelial cells.

Body weight measurements made on both the control and exposed animals throughout the exposure period indicated that the animals in all groups increased in body weights. Analysis of these data did not reveal any significant differences in the rate of growth between the control and exposed animals. No meaningful differences were detected in terminal body weights, organ weights, or organ/body weight ratios between the control and exposed groups.

Hematological, clinical biochemical, and arterial blood gas measurements were made on both the control and exposed animals pre-exposure and periodically throughout the exposure period. No trends were detected in any of these variables in the exposed animals. No meaningful differences were detected between the control and exposed animals.



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Appendix C - Data compilations and summary of statistical analysis for

Statistical Grouping C, comprised of the following:

Group I - Control, Group II - 9.70 ppm SO₂, Group III -
0.51 mg/m³ PbClBr, and Group IV - 9.93 ppm SO₂ +
0.50 mg/m³ PbClBr.

Table 1 - Monthly means and the grand mean for the analytical concentrations of sulfur dioxide for Group II.

Date	n	$\bar{x}$ ppm	S.D.
3/31/68 - 4/30/68	31	8.2971	1.8973
5/ 1/68 - 5/31/68	31	8.6948	2.1871
6/ 1/68 - 6/30/68	30	9.2770	1.4754
7/ 1/68 - 7/31/68	31	9.5377	1.1408
8/ 1/68 - 8/31/68	31	7.8032	2.2194
9/ 1/68 - 9/30/68	30	9.4020	1.6718
10/ 1/68 - 10/31/68	31	9.7019	1.9957
11/ 1/68 - 11/30/68	30	10.3617	0.9926
12/ 1/68 - 12/31/68	31	9.6352	1.1671
1/ 1/69 - 1/31/69	31	8.0226	2.1791
2/ 1/69 - 2/28/69	28	9.8011	0.7511
3/ 1/69 - 3/31/69	31	9.5323	1.3048
4/ 1/69 - 4/30/69	30	10.8390	0.4810
5/ 1/69 - 5/31/69	31	10.1565	0.6112
6/ 1/69 - 6/30/69	30	9.9767	0.7278
7/ 1/69 - 7/31/69	31	10.2965	0.7100
8/ 1/69 - 8/31/69	31	10.4761	0.6406
9/ 1/69 - 9/30/69	30	9.7290	0.5017
10/ 1/69 - 10/31/69	31	10.0545	0.4867
11/ 1/69 - 11/30/69	30	10.1233	0.4409
12/ 1/69 - 12/31/69	31	10.3842	0.5963
1/ 1/70 - 1/31/70	31	10.3281	0.6138
2/ 1/70 - 2/28/70	28	10.1696	0.5316
3/ 1/70 - 4/ 2/70	31	10.7761	0.6594

N = 24
 $\bar{X}$ = 9.70
 S.D. = 1.10

Table 2 - Monthly means and the grand mean for the analytical concentrations of lead chlorobromide in Group III.

Date	n	$\bar{x}$ mg/m ³	S.D.
5/11/68 - 5/31/68	20	0.8570	1.0552
6/ 1/68 - 6/30/68	30	0.4743	0.6379
7/ 1/68 - 7/31/68	31	0.4565	0.3048
8/ 1/68 - 8/31/68	31	0.6022	0.1088
9/ 1/68 - 9/30/68	30	0.5773	0.1526
10/ 1/68 - 10/31/68	31	0.5074	0.1497
11/ 1/68 - 11/30/68	30	0.4286	0.1944
12/ 1/68 - 12/31/68	31	0.4638	0.1819
1/ 1/69 - 1/31/69	31	0.4752	0.1339
2/ 1/69 - 2/28/69	28	0.6154	0.7173
3/ 1/69 - 3/31/69	31	0.5677	0.1515
4/ 1/69 - 4/30/69	30	0.5147	0.2131
5/ 1/69 - 5/31/69	31	0.7770	0.1710
6/ 1/69 - 6/30/69	30	0.5503	0.1740
7/ 1/69 - 7/31/69	31	0.5597	0.2216
8/ 1/69 - 8/31/69	31	0.5010	0.1545
9/ 1/69 - 9/30/69	30	0.4737	0.2049
10/ 1/69 - 10/31/69	31	0.5352	0.2722
11/ 1/69 - 11/30/69	30	0.4930	0.0363
12/ 1/69 - 12/31/69	31	0.3871	0.1065
1/ 1/70 - 1/31/70	31	0.4052	0.2503
2/ 1/70 - 2/28/70	28	0.5100	0.3669
3/ 1/70 - 3/31/70	31	0.5561	0.2526
4/ 1/70 - 4/30/70	30	0.3070	0.5232
5/ 1/70 - 5/ 5/70	5	0.1080	0.0295

N = 25

$\bar{X}$ = 0.51

S.D. = 0.27

Table 3 - Monthly means and the grand mean for the analytical concentrations of sulfur dioxide and lead chlorobromide for Group IV.

Date	n	SO ₂		PbClBr	
		$\bar{x}$ ppm	S.D.	$\bar{x}$ mg/m ³	S.D.
6/ 1/68 - 6/30/68	30	9.0860	1.2098	0.7460	0.6084
7/ 1/68 - 7/31/68	31	9.4800	1.5272	0.6381	0.3021
8/ 1/68 - 8/31/68	31	8.1126	2.3330	0.5897	0.1578
9/ 1/68 - 9/30/68	30	8.1710	1.8994	0.4690	9.3260
10/ 1/68 - 10.31/68	31	9.8820	9.2737	0.4271	0.1582
11/ 1/68 - 11/30/68	30	9.8613	0.9160	0.3920	0.1834
12/ 1/68 - 12/31/68	31	10.1381	1.2822	0.4500	0.1752
1/ 1/69 - 1/31/69	31	8.1694	2.2516	0.4755	0.1776
2/ 1/69 - 2/28/69	28	9.9996	0.9223	0.5825	0.3086
3/ 1/69 - 3/31/69	31	9.8535	1.4923	0.6377	0.2419
4/ 1/69 - 4/30/69	30	10.6361	2.0651	0.5557	0.2620
5/ 1/69 - 5/31/69	31	10.2061	0.6014	0.6194	0.1859
6/ 1/69 - 6/30/69	30	10.0123	0.7646	0.6340	0.2501
7/ 1/69 - 7/31/69	31	10.2297	0.7385	0.4252	0.1405
8/ 1/69 - 8/31/69	31	10.5742	0.6935	0.4516	0.2649
9/ 1/69 - 9/30/69	30	9.9700	0.5091	0.4090	0.1720
10/ 1/69 - 10/31/69	31	10.1168	9.4745	0.3925	0.2516
11/ 1/69 - 11/30/69	30	10.2610	0.3675	0.4333	0.1563
12/ 1/69 - 12/31/69	31	10.4919	0.3204	0.5413	0.2833
1/ 1/70 - 1/31/70	31	10.5181	0.4787	0.5906	0.3867
2/ 1/70 - 2/28/70	28	10.4392	0.3408	0.5257	0.9777
3/ 1/70 - 3/31/70	31	10.4284	0.4740	0.5903	0.2595
4/ 1/70 - 4/30/70	30	10.8520	0.2919	0.2017	0.0730
5/ 1/70 - 5/12/70	12	10.8500	0.4373	0.2417	0.1083

N = 24
 $\bar{X}$ = 9.93
S.D. = 1.03

N = 24
 $\bar{X}$ = 0.50
S.D. = 0.27

Table 4 - Summary of statistical analyses of body weight data for Statistical Grouping C, comprised of the following: Group I - Control, Group II - 9.70 ppm SO₂, Group III - 0.51 mg/m³ PbcIBr, and Group IV - 9.93 ppm SO₂ + 0.50 mg/m³ PbcIBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	2.908	9.693 x 10 ⁻¹	0.96	-
Error Deviation	886	8.892 x 10 ²	1.004	-	-

FIRST DEGREE POLYNOMIAL REGRESSION COEFFICIENTS					
GROUPS	REGRESSION COEFFICIENTS		S.E.	SV, X	n
	A	B			
I	2.63 ± 0.052	1.64 x 10 ⁻² ± 8.93 x 10 ⁻⁴		0.14	33
II	2.85 ± 0.053	1.13 x 10 ⁻² ± 8.91 x 10 ⁻⁴		0.14	30
III	2.61 ± 0.046	1.53 x 10 ⁻² ± 8.02 x 10 ⁻⁴		0.13	30
IV	2.62 ± 0.055	1.45 x 10 ⁻² ± 9.23 x 10 ⁻⁴		0.14	31

Table 5 - Summary of statistical analyses of total respiratory system flow resistance during inspiration data for Statistical Grouping C, comprised of the following: Group I - Control, Group II - 9.70 ppm SO₂, Group III - 0.51 mg/m³ PbClBr, and Group IV - 9.93 ppm SO₂ + 0.50 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	1.045 x 10 ⁻³	3.482 x 10 ⁻⁴	2.69	Yes
Error Deviation	1119	1.446 x 10 ⁻¹	1.292 x 10 ⁻⁴	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS						
GROUPS	REGRESSION COEFFICIENTS ± S.E.				SY.X	r
	A	B	C	D		
I	0.044 ± 0.0033	2.12 x 10 ⁻⁴ ± 3.81 x 10 ⁻⁴	-9.72 x 10 ⁻⁶ ± 9.30 x 10 ⁻⁶	8.10 x 10 ⁻⁸ ± 6.10 x 10 ⁻⁸	0.008	0.37
II	0.043 ± 0.0029	-7.21 x 10 ⁻⁵ ± 3.34 x 10 ⁻⁴	1.50 x 10 ⁻⁶ ± 8.10 x 10 ⁻⁶	-7.00 x 10 ⁻⁹ ± 5.30 x 10 ⁻⁸	0.007	0.08
III	0.053 ± 0.0026	-5.51 x 10 ⁻⁴ ± 3.01 x 10 ⁻⁴	5.41 x 10 ⁻⁶ ± 7.35 x 10 ⁻⁶	-2.00 x 10 ⁻⁹ ± 4.80 x 10 ⁻⁸	0.006	0.65
IV	0.046 ± 0.002	-2.45 x 10 ⁻⁴ ± 3.36 x 10 ⁻⁴	4.49 x 10 ⁻⁶ ± 8.56 x 10 ⁻⁶	-1.90 x 10 ⁻⁸ ± 5.80 x 10 ⁻⁸	0.006	0.25

Table 6 - Summary of statistical analyses of total respiratory system flow resistance during expiration data for Statistical Grouping C, comprised of the following: Group I - Control, Group II - 9.70 ppm SO₂, Group III - 0.51 mg/m³ PbClBr, and Group IV - 9.93 ppm SO₂ + 0.50 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	1.157 x 10 ⁻³	3.857 x 10 ⁻⁴	3.84	Yes
Error Deviation	1119	1.124 x 10 ⁻¹	1.005 x 10 ⁻⁴	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.				Sy.x	n	r
	A	B	C	D			
I	0.042 ± 0.0028	-2.07 x 10 ⁻⁴ ± 3.26 x 10 ⁻⁴	-1.34 x 10 ⁻⁶ ± 7.97 x 10 ⁻⁶	2.90 x 10 ⁻⁸ ± 5.20 x 10 ⁻⁸	0.007	39	0.55
II	0.040 ± 0.0025	-3.48 x 10 ⁻⁴ ± 2.90 x 10 ⁻⁴	5.82 x 10 ⁻⁶ ± 7.02 x 10 ⁻⁶	-2.90 x 10 ⁻⁸ ± 4.60 x 10 ⁻⁸	0.006	38	0.36
III	0.046 ± 0.0023	-6.02 x 10 ⁻⁴ ± 2.70 x 10 ⁻⁴	7.29 x 10 ⁻⁶ ± 6.61 x 10 ⁻⁶	1.90 x 10 ⁻⁶ ± 4.30 x 10 ⁻⁸	0.005	39	0.67
IV	0.040 ± 0.0024	-3.82 x 10 ⁻⁴ ± 2.86 x 10 ⁻⁴	7.76 x 10 ⁻⁶ ± 7.29 x 10 ⁻⁶	-4.20 x 10 ⁻⁸ ± 4.90 x 10 ⁻⁸	0.005	36	0.30

Table 7 - Summary of statistical analyses of tidal volume data for Statistical Grouping C, comprised of the following: Group I - Control, Group II - 9.70 ppm SO₂, Group III - 0.51 mg/m³ PbClBr, and Group IV - 9.93 ppm SO₂ + 0.50 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	9.489 x 10 ⁺¹	3.163 x 10 ⁺¹	0.26	-
Error Deviation	879	1.047 x 10 ⁺⁵	1.191 x 10 ⁺²	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.					Sy.x	n	r
	A	B	C	D				
I	28.72 ± 1.92	2.52 x 10 ⁻¹ ± 1.88 x 10 ⁻¹	-2.46 x 10 ⁻³ ± 4.42 x 10 ⁻³	1.16 x 10 ⁻⁵ ± 2.84 x 10 ⁻⁵		3.48	32	0.77
II	32.29 ± 2.02	3.08 x 10 ⁻¹ ± 1.94 x 10 ⁻¹	-4.07 x 10 ⁻³ ± 4.54 x 10 ⁻³	2.04 x 10 ⁻⁵ ± 2.90 x 10 ⁻⁵		3.67	32	0.68
III	31.10 ± 1.75	1.64 x 10 ⁻² ± 1.72 x 10 ⁻¹	5.87 x 10 ⁻⁴ ± 4.10 x 10 ⁻³	3.80 x 10 ⁻⁶ ± 2.64 x 10 ⁻⁵		3.20	31	0.79
IV	27.50 ± 1.70	3.50 x 10 ⁻¹ ± 1.64 x 10 ⁻¹	-3.28 x 10 ⁻³ ± 3.91 x 10 ⁻³	8.10 x 10 ⁻⁶ ± 2.57 x 10 ⁻⁵		2.81	28	0.82

Table 8 - Summary of statistical analyses of respiratory rate data for Statistical Grouping C, comprised of the following: Group I - Control, Group II - 9.70 ppm SO₂, Group III - 0.51 mg/m³ PbcIbR, and Group IV - 9.93 ppm SO₂ + 0.50 mg/m³ PbcIbR.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	7.452 x 10 ⁺²	2.484 x 10 ⁺²	3.93	Yes
Error Deviation	879	5.551 x 10 ⁺⁴	6.315 x 10 ⁺¹	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.					SY.X	n	r
	A	B	C	D	%			
I	40.74 ± 1.26	3.16 x 10 ⁻¹ ± 1.23 x 10 ⁻¹	-9.30 x 10 ⁻³ ± 2.90 x 10 ⁻³	5.63 x 10 ⁻⁵ ± 1.86 x 10 ⁻⁵		2.29	32	0.84
II	38.90 ± 1.38	2.08 x 10 ⁻¹ ± 1.32 x 10 ⁻¹	-5.91 x 10 ⁻³ ± 3.09 x 10 ⁻³	3.58 x 10 ⁻⁵ ± 1.98 x 10 ⁻⁵		2.50	32	0.63
III	37.85 ± 1.83	2.67 x 10 ⁻¹ ± 1.80 x 10 ⁻¹	-4.08 x 10 ⁻³ ± 4.28 x 10 ⁻³	1.39 x 10 ⁻⁵ ± 2.76 x 10 ⁻⁵		3.34	31	0.51
IV	42.94 ± 1.18	1.40 x 10 ⁻¹ ± 1.13 x 10 ⁻¹	-4.12 x 10 ⁻³ ± 2.70 x 10 ⁻³	2.38 x 10 ⁻⁵ ± 1.78 x 10 ⁻⁵		1.94	28	0.71

Table 9 - Summary of statistical analysis of dynamic compliance of the lung data for Statistical Grouping C, comprised of the following: Group I - Control, Group II - 9.70 ppm SO₂, Group III - 0.51 mg/m³ PbClBr, and Group IV - 9.93 ppm SO₂ + 0.50 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	5.902 x 10 ⁻¹	1.967 x 10 ⁻¹	3.54	Yes
Error Deviation	879	4.889 x 10 ⁻³	5.563	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.				Sy.x	n	r
	A	B	C	D			
I	6.01 ± 0.46	1.83 x 10 ⁻² ± 4.55 x 10 ⁻²	-1.88 x 10 ⁻⁴ ± 1.07 x 10 ⁻³	1.30 x 10 ⁻⁶ ± 6.90 x 10 ⁻⁶	0.84	32	0.43
II	8.07 ± 0.87	-6.98 x 10 ⁻³ ± 8.37 x 10 ⁻²	4.10 x 10 ⁻⁴ ± 1.96 x 10 ⁻³	-3.30 x 10 ⁻⁶ ± 1.25 x 10 ⁻⁵	1.58	32	0.11
III	6.09 ± 0.57	6.22 x 10 ⁻² ± 5.65 x 10 ⁻²	-1.12 x 10 ⁻³ ± 1.34 x 10 ⁻³	6.80 x 10 ⁻⁶ ± 8.70 x 10 ⁻⁶	1.05	31	0.45
IV	5.49 ± 0.43	-1.64 x 10 ⁻² ± 4.13 x 10 ⁻²	1.35 x 10 ⁻³ ± 9.87 x 10 ⁻⁴	-1.01 x 10 ⁻⁵ ± 6.50 x 10 ⁻⁶	0.71	28	0.80

Table 10 - Summary of statistical analyses of pulmonary flow resistance data for Statistical Grouping C, comprised of the following: Group I - Control, Group II - 9.70 ppm SO₂, Group III - 0.51 mg/m³ PbClBr, and Group IV - 9.93 ppm SO₂ + 0.50 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	1.755 x 10 ⁻³	5.850 x 10 ⁻⁴	4.05	Yes
Error Deviation	879	1.269 x 10 ⁻¹	1.443 x 10 ⁻⁴	-	-

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THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.				Sv.x	n	r
	A	B	C	D			
I	0.024 ± 0.0036	7.84 x 10 ⁻⁵ ± 3.53 x 10 ⁻⁴	8.71 x 10 ⁻⁷ ± 8.32 x 10 ⁻⁶	-1.80 x 10 ⁻⁸ ± 5.30 x 10 ⁻⁸	0.006	32	0.28
II	0.019 ± 0.0032	3.54 x 10 ⁻⁴ ± 3.13 x 10 ⁻⁴	-9.10 x 10 ⁻⁶ ± 7.32 x 10 ⁻⁶	5.29 x 10 ⁻⁸ ± 4.70 x 10 ⁻⁸	0.006	32	0.48
III	0.025 ± 0.0039	8.94 x 10 ⁻⁶ ± 3.82 x 10 ⁻⁴	-7.73 x 10 ⁻⁷ ± 9.10 x 10 ⁻⁶	-3.00 x 10 ⁻⁹ ± 5.90 x 10 ⁻⁸	0.007	31	0.45
IV	0.026 ± 0.0031	2.72 x 10 ⁻⁴ ± 2.97 x 10 ⁻⁴	-9.95 x 10 ⁻⁶ ± 7.09 x 10 ⁻⁶	6.60 x 10 ⁻⁸ ± 4.70 x 10 ⁻⁸	0.005	28	0.65

Table 11 - Summary of statistical analyses of work of breathing during inspiration per ml tidal volume data for Statistical Grouping C, comprised of the following: Group I - Control, Group II - 9.70 ppm SO₂, Group III - 0.51 mg/m³ PbClBr, and Group IV - 9.93 ppm SO₂ + 0.50 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	1.701 × 10 ⁺¹	5.670	3.39	Yes
Error Deviation	878	1.457 × 10 ⁺³	1.671	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.					Sy.x	n	r
	A	B	C	D	D			
I	3.94 ± 0.30	-2.00 × 10 ⁻² ± 2.97 × 10 ⁻⁴	5.07 × 10 ⁻⁴ ± 7.00 × 10 ⁻⁴	-2.90 × 10 ⁻⁶ ± 4.50 × 10 ⁻⁶	-2.90 × 10 ⁻⁶ ± 4.50 × 10 ⁻⁶	0.55	32	0.25
II	3.36 ± 0.42	1.74 × 10 ⁻² ± 4.05 × 10 ⁻²	-6.45 × 10 ⁻⁴ ± 9.48 × 10 ⁻⁴	5.20 × 10 ⁻⁶ ± 6.10 × 10 ⁻⁶	5.20 × 10 ⁻⁶ ± 6.10 × 10 ⁻⁶	0.77	32	0.27
III	4.13 ± 0.36	-7.57 × 10 ⁻² ± 3.54 × 10 ⁻²	1.49 × 10 ⁻³ ± 8.43 × 10 ⁻³	-7.90 × 10 ⁻⁶ ± 5.40 × 10 ⁻⁶	-7.90 × 10 ⁻⁶ ± 5.40 × 10 ⁻⁶	0.66	31	0.46
IV	4.23 ± 0.40	-1.94 × 10 ⁻⁴ ± 3.86 × 10 ⁻²	-3.73 × 10 ⁻⁴ ± 9.23 × 10 ⁻⁴	3.30 × 10 ⁻⁶ ± 6.10 × 10 ⁻⁶	3.30 × 10 ⁻⁶ ± 6.10 × 10 ⁻⁶	0.66	28	0.41

Table 12 - Summary of statistical analyses of work of breathing during expiration per ml tidal volume data for Statistical Grouping C, comprised of the following: Group I - Control, Group II - 9.70 ppm SO₂, Group III - 0.51 mg/m³ PClBr, and Group IV - 9.93 ppm SO₂ + 0.50 mg/m³ PClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	9.244 x 10 ⁻¹	3.081 x 10 ⁻¹	0.99	-
Error Deviation	878	2.723 x 10 ⁺²	3.101 x 10 ⁻¹	-	-

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THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.					n	r
	A	B	C	D	Sy.x		
I	1.85 ± 0.16	-2.66 x 10 ⁻² ± 7.60 x 10 ⁻⁴	5.49 x 10 ⁻⁴ ± 3.76 x 10 ⁻⁴	-3.00 x 10 ⁻⁶ ± 2.40 x 10 ⁻⁶	0.30	32	0.36
II	1.60 ± 0.15	-1.55 x 10 ⁻² ± 7.50 x 10 ⁻⁴	2.82 x 10 ⁻⁴ ± 3.50 x 10 ⁻⁴	-1.20 x 10 ⁻⁶ ± 2.20 x 10 ⁻⁶	0.28	32	0.34
III	1.73 ± 0.16	-2.15 x 10 ⁻² ± 1.57 x 10 ⁻²	3.97 x 10 ⁻⁴ ± 3.74 x 10 ⁻⁴	-1.80 x 10 ⁻⁶ ± 2.40 x 10 ⁻⁶	0.29	31	0.39
IV	1.78 ± 0.16	-3.43 x 10 ⁻³ ± 1.54 x 10 ⁻²	-3.64 x 10 ⁻⁵ ± 3.69 x 10 ⁻⁴	6.00 x 10 ⁻⁷ ± 2.40 x 10 ⁻⁶	0.26	28	0.27

Table 13 - Summary of statistical analyses of diffusing capacity of the lung for carbon monoxide data for Statistical Grouping C, comprised of the following: Group I - Control, Group II - 9.70 ppm SO₂, Group III - 0.51 mg/m³ PbClBr, and Group IV - 9.93 ppm SO₂ + 0.50 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p < .05
Non-Parallelism	3	9.553×10^{-2}	3.184×10^{-2}	1.29	-
Error Deviation	886	2.185×10^{-1}	2.466×10^{-2}	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.					SV.x	n	r
	A	B	C	D	D			
I	0.62 ± 0.031	3.04×10^{-3} ± 2.91×10^{-3}	-2.49×10^{-5} ± 7.00×10^{-5}	1.50×10^{-7} ± 4.60×10^{-7}		0.052	33	0.78
II	0.72 ± 0.042	-1.08×10^{-3} ± 4.10×10^{-3}	4.16×10^{-5} ± 9.69×10^{-5}	-1.90×10^{-7} ± 6.30×10^{-7}		0.069	30	0.58
III	0.67 ± 0.052	-3.33×10^{-3} ± 4.83×10^{-3}	1.26×10^{-4} ± 1.16×10^{-4}	-7.50×10^{-7} ± 7.70×10^{-7}		0.087	33	0.68
IV	0.70 ± 0.034	-1.90×10^{-3} ± 3.29×10^{-3}	7.41×10^{-5} ± 7.87×10^{-5}	-3.70×10^{-7} ± 5.20×10^{-7}		0.057	31	0.78

Table 14 - Summary of statistical analyses of number of breaths to 1% nitrogen data for Statistical Grouping C, comprised of the following: Group I - Control, Group II - 9.70 ppm SO₂, Group III - 0.51 mg/m³ PbClBr, and Group IV - 9.93 ppm SO₂ + 0.50 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	5.188 x 10 ⁺²	1.729 x 10 ⁺²	1.08	-
Error Deviation	884	1.413 x 10 ⁺⁵	1.598 x 10 ⁺²	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.					Sy.x	n	r
	A	B	C	D				
I	42.85 ± 3.42	8.85 x 10 ⁻² ± 3.26 x 10 ⁻¹	1.08 x 10 ⁻³ ± 7.83 x 10 ⁻³	-2.10 x 10 ⁻⁵ ± 5.20 x 10 ⁻⁵		5.69	32	0.33
II	41.79 ± 3.01	2.96 x 10 ⁻¹ ± 2.95 x 10 ⁻¹	-6.92 x 10 ⁻³ ± 6.99 x 10 ⁻³	4.90 x 10 ⁻⁵ ± 4.50 x 10 ⁻⁵		4.96	30	0.44
III	44.77 ± 3.08	2.51 x 10 ⁻¹ ± 2.93 x 10 ⁻¹	1.16 x 10 ⁻³ ± 7.06 x 10 ⁻³	-3.40 x 10 ⁻⁵ ± 4.70 x 10 ⁻⁵		5.16	32	0.64
IV	37.88 ± 2.36	1.85 x 10 ⁻¹ ± 2.22 x 10 ⁻¹	2.59 x 10 ⁻³ ± 5.39 x 10 ⁻³	-4.70 x 10 ⁻⁵ ± 3.60 x 10 ⁻⁵		3.96	31	0.73

Table 15 - Summary of statistical analyses of respiratory rate (during oxygen breathing) data for Statistical Grouping C, comprised of the following: Group I - Control; Group II - 9.70 ppm SO₂, Group III - 0.51 mg/m³ PbClBr, and Group IV - 9.93 ppm SO₂ + 0.50 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	5.070 × 10 ⁺²	1.690 × 10 ⁺²	2.45	-
Error Deviation	884	6.087 × 10 ⁺⁴	6.886 × 10 ⁺¹	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.					n	r
	A	B	C	D	Sy.x		
I	34.46 ± 1.11	2.49 × 10 ⁻¹ ± 1.06 × 10 ⁻¹	-9.27 × 10 ⁻³ ± 2.54 × 10 ⁻³	6.52 × 10 ⁻⁵ ± 1.68 × 10 ⁻⁵	1.84	32	0.86
II	34.42 ± 1.51	2.48 × 10 ⁻¹ ± 1.48 × 10 ⁻¹	-7.12 × 10 ⁻³ ± 3.51 × 10 ⁻³	4.36 × 10 ⁻⁵ ± 2.28 × 10 ⁻⁵	2.50	30	0.70
III	33.38 ± 1.80	1.91 × 10 ⁻¹ ± 1.71 × 10 ⁻¹	-2.86 × 10 ⁻³ ± 4.13 × 10 ⁻³	7.40 × 10 ⁻⁶ ± 2.72 × 10 ⁻⁶	3.02	32	0.52
IV	38.94 ± 1.77	-6.47 × 10 ⁻² ± 1.67 × 10 ⁻¹	8.83 × 10 ⁻⁴ ± 4.05 × 10 ⁻³	-5.40 × 10 ⁻⁶ ± 2.68 × 10 ⁻⁶	2.97	31	0.30

Table 16 - Summary of statistical analyses of cumulative tidal volume to 1% nitrogen data for Statistical Grouping C, comprised of the following: Group I - Control, Group II - 9.70 ppm SO₂, Group III - 0.51 mg/m³ PbClBr, and Group IV - 9.93 ppm SO₂ + 0.50 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	3.947 x 10 ⁻¹	1.316 x 10 ⁻¹	0.81	-
Error Deviation	884	1.426 x 10 ⁻²	1.613 x 10 ⁻¹	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.					n	r
	A	B	C	D	Sy.X		
I	1.35 ± 0.094	5.79 x 10 ⁻³ ± 8.95 x 10 ⁻³	-1.38 x 10 ⁻⁵ ± 2.15 x 10 ⁻⁴	0.00 ± 1.40 x 10 ⁻⁶	0.16	32	0.70
II	1.53 ± 0.108	1.50 x 10 ⁻³ ± 1.06 x 10 ⁻²	5.12 x 10 ⁻⁵ ± 2.52 x 10 ⁻⁴	-4.00 x 10 ⁻⁷ ± 1.60 x 10 ⁻⁶	0.18	30	0.52
III	1.52 ± 0.074	4.55 x 10 ⁻⁴ ± 7.04 x 10 ⁻³	2.09 x 10 ⁻⁴ ± 1.70 x 10 ⁻⁴	-1.80 x 10 ⁻⁶ ± 1.10 x 10 ⁻⁶	0.12	32	0.82
IV	1.25 ± 0.081	-2.85 x 10 ⁻³ ± 7.65 x 10 ⁻³	3.42 x 10 ⁻⁴ ± 1.85 x 10 ⁻⁴	-2.90 x 10 ⁻⁶ ± 1.20 x 10 ⁻⁶	0.14	31	0.81

Table 17 - Summary of statistical analyses of tidal volume (during oxygen breathing) data for Statistical Grouping C, comprised of the following: Group I - Control, Group II - 9.70 ppm SO₂, Group III - 0.51 mg/m³ PbClBr, and Group IV - 9.93 ppm SO₂ + 0.50 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	1.125 x 10 ⁻³	3.751 x 10 ⁻²	4.00	Yes
Error Deviation	884	8.284 x 10 ⁻⁴	9.371 x 10 ⁻⁷	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.					SY.X	n	r
	A	B	C	D				
I	39.08 ± 2.58	2.20 x 10 ⁻¹ ± 2.47 x 10 ⁻¹	-5.34 x 10 ⁻³ ± 5.92 x 10 ⁻³	4.68 x 10 ⁻⁵ ± 3.91 x 10 ⁻⁵		4.30	32	0.70
II	45.45 ± 2.70	-1.52 x 10 ⁻¹ ± 2.07 x 10 ⁻¹	5.46 x 10 ⁻³ ± 4.89 x 10 ⁻³	-4.01 x 10 ⁻⁵ ± 3.18 x 10 ⁻⁵		3.47	30	0.38
III	43.09 ± 2.17	-1.77 x 10 ⁻¹ ± 2.07 x 10 ⁻¹	3.84 x 10 ⁻³ ± 4.97 x 10 ⁻³	-1.63 x 10 ⁻⁵ ± 3.28 x 10 ⁻⁵		5.64	32	0.53
IV	41.72 ± 1.93	-2.38 x 10 ⁻¹ ± 1.82 x 10 ⁻¹	6.50 x 10 ⁻³ ± 4.40 x 10 ⁻³	-3.35 x 10 ⁻⁵ ± 2.92 x 10 ⁻⁵		3.24	31	0.76

Table 18 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for hematoocrit (Hct. - percent) for male and female monkeys in Statistical Grouping C.

Groups	Pre-exposure -8	Time-Weeks			104
		4	16	68	
I - Control	36.4 (0.8)	36.0 (1.0)	33.1 (1.0)	37.3 (1.0)	36.7 (0.8)
II - 9.70 ppm SO ₂	35.0 (0.7)	35.0 (0.6)	34.0 (0.6)	36.4 (0.6)	36.6 (0.6)
III - 0.51 mg/m ³ PbClBr	32.3 (0.8)	35.8 (0.8)	34.3 (0.9)	35.4 (1.1)	36.2 (0.9)
IV - 9.93 ppm SO ₂ + 0.50 mg m ³ PbClBr	34.2 (1.2)	33.8 (1.4)	34.1 (1.1)	37.8 (1.2)	38.9 (1.2)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Pre-exposure -8	Time-Weeks			104
		4	16	68	
Pb	SIG	N.S.	N.S.	N.S.	N.S.
SO ₂	N.S.	N.S.	N.S.	N.S.	N.S.
Interaction	N.S.	N.S.	N.S.	N.S.	N.S.

Table 19 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for hemoglobin (Hgb. - grams percent.) for male and female monkeys in Statistical Grouping C.

Groups	Pre-exposure -8	Time-Weeks			
		4	16	68	104
I - Control	10.5 (0.3)	11.0 (0.3)	11.2 (0.2)	10.7 (0.3)	11.7 (0.3)
II - 9.70 ppm SO ₂	10.5 (0.2)	10.6 (0.2)	10.1 (0.2)	11.0 (0.2)	10.9 (0.2)
III - 0.51 mg/m ³ PbClBr	10.2 (0.2)	9.8 (0.2)	10.4 (0.2)	10.4 (0.3)	10.6 (0.3)
IV - 9.93 ppm SO ₂ + 0.50 mg/m ³ PbClBr	9.8 (0.3)	11.1 (0.5)	11.1 (0.3)	11.2 (0.4)	11.2 (0.4)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Pre-exposure -8	Time-Weeks			
		4	16	68	104
Pb	SIG	N.S.	N.S.	N.S.	N.S.
SO ₂	N.S.	N.S.	N.S.	N.S.	N.S.
Interaction	N.S.	SIG	SIG	N.S.	SIG

Table 20 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for total erythrocyte count (RBC - 106/cmm) for male and female monkeys in Statistical Grouping C.

Groups	Time-Weeks			
	Pre-exposure -8	4	16	68
I - Control	5.44 (0.09)	5.44 (0.18)	5.70 (0.22)	5.10 (0.13)
II - 9.70 ppm SO ₂	5.08 (0.08)	5.20 (0.14)	4.98 (0.12)	5.39 (0.11)
III - 0.51 mg/m ³ PbClBr	5.13 (0.18)	4.89 (0.20)	5.39 (0.30)	5.64 (0.23)
IV - 9.93 ppm SO ₂ + 0.50 mg/m ³ PbClBr	5.00 (0.21)	5.20 (0.17)	5.06 (0.23)	5.52 (0.25)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks			
	Pre-exposure -8	4	16	68
Pb	SIG	N.S.	N.S.	N.S.
SO ₂	SIG	N.S.	SIG	SIG
Interaction	N.S.	N.S.	N.S.	N.S.

Table 21 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for total leukocyte count (WBC - per cmm) for male and female monkeys in Statistical Grouping C.

Groups	Time-Weeks			
	Pre-exposure -8	4	16	68
I - Control	7240 (840)	7170 (290)	8670 (710)	8220 (680)
II - 9.70 ppm SO ₂	9140 (720)	10110 (1160)	14260 (1210)	11680 (680)
III - 0.51 mg/m ³ PbClBr	8430 (860)	11040 (3060)	9700 (930)	9110 (850)
IV - 9.93 ppm SO ₂ + 0.50 mg/m ³ PbClBr	6430 (940)	8510 (700)	10530 (940)	9050 (730)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks			
	Pre-exposure -8	4	16	68
Pb	N.S.	N.S.	N.S.	N.S.
SO ₂	N.S.	N.S.	SIG	SIG
Interaction	SIG	N.S.	SIG	SIG

Table 22 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for blood glucose (Glu. - mg percent) for male and female monkeys in Statistical Grouping C.

Groups	Time-Weeks				
	Pre-exposure -8	4	16	68	104
I - Control	59.3 (3.3)	59.5 (3.3)	69.0 (4.4)	97.3 (5.3)	82.4 (7.5)
II - 9.70 ppm SO ₂	61.3 (1.6)	75.3 (3.6)	76.8 (5.7)	86.6 (6.0)	71.6 (5.3)
III - 0.51 mg/m ³ PbClBr	68.3 (2.9)	52.0 (3.0)	80.0 (2.2)	93.4 (3.5)	87.3 (5.2)
IV - 9.93 ppm SO ₂ + 0.50 mg/m ³ PbClBr	72.8 (2.1)	104.7 (9.0)	75.2 (6.9)	63.4 (2.7)	80.5 (7.6)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks				
	Pre-exposure -8	4	16	68	104
Pb	SIG	N.S.	N.S.	SIG	N.S.
SO ₂	N.S.	SIG	N.S.	SIG	N.S.
Interaction	N.S.	SIG	N.S.	SIG	N.S.

Table 23 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for blood urea nitrogen (BUN - mg percent) for male and female monkeys in Statistical Grouping C.

Groups	Time-Weeks			
	Pre-exposure -8	4	16	68
I - Control	16.3 (1.0)	19.2 (1.4)	17.0 (0.6)	22.6 (0.7)
II - 9.70 ppm SO ₂	18.7 (1.5)	14.1 (1.0)	15.4 (0.7)	19.1 (1.8)
III - 0.51 mg/m ³ PbClBr	14.4 (0.6)	15.8 (0.5)	8.8 (0.9)	22.6 (1.6)
IV - 9.93 ppm SO ₂ + 0.50 mg/m ³ PbClBr	17.4 (1.0)	25.5 (3.5)	28.8 (1.6)	25.9 (1.8)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks			
	Pre-exposure -8	4	16	68
Pb	N.S.	SIG	SIG	SIG
SO ₂	SIG	N.S.	SIG	N.S.
Interaction	N.S.	SIG	SIG	SIG

Table 24 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for total serum bilirubin (mg percent) for male and female monkeys in Statistical Grouping C.

Groups	Time-Weeks			
	Pre-exposure -8	4	16	68
I - Control	0.27 (0.03)	0.26 (0.02)	0.26 (0.02)	0.29 (0.03)
II - 9.70 ppm SO ₂	0.27 (0.02)	0.21 (0.02)	0.41 (0.04)	0.24 (0.02)
III - 0.51 mg/m ³ PbClBr	0.18 (0.01)	0.28 (0.02)	0.28 (0.02)	0.27 (0.01)
IV - 9.93 ppm SO ₂ + 0.50 mg/m ³ PbClBr	0.60 (0.08)	0.70 (0.12)	0.40 (0.06)	0.54 (0.05)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks			
	Pre-exposure -8	4	16	68
Pb	SIG	SIG	N.S.	N.S.
SO ₂	SIG	SIG	SIG	N.S.
Interaction	SIG	SIG	N.S.	SIG

Table 25 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for total serum protein (grams percent) for male and female monkeys in Statistical Grouping C.

Groups	Time-Weeks			
	Pre-exposure -8	4	16	68
I - Control	7.30 (0.13)	7.76 (0.13)	8.24 (0.10)	7.44 (0.13)
II - 9.70 ppm SO ₂	7.57 (0.12)	7.30 (0.12)	7.61 (0.06)	7.61 (0.06)
III - 0.51 mg/m ³ PbClBr	7.53 (0.17)	7.74 (0.19)	7.75 (0.22)	7.00 (0.13)
IV - 9.93 ppm SO ₂ + 0.50 mg/m ³ PbClBr	7.62 (0.08)	8.02 (0.14)	8.00 (0.20)	7.56 (0.19)

Comparison of Experimental Treatment Effects, $p \leq .05$

Source of Variation	Time-Weeks			
	Pre-exposure -8	4	16	68
Pb	N.S.	SIG	N.S.	N.S.
SO ₂	N.S.	N.S.	N.S.	SIG
Interaction	N.S.	SIG	SIG	N.S.

Table 26 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for serum albumin (grams percent) for male and female monkeys in Statistical Grouping C.

Groups	Time-Weeks			
	Pre-exposure -8	4	16	68
I - Control	2.56 (0.14)	2.58 (0.05)	3.11 (0.06)	2.45 (0.11)
II - 0.70 ppm SO ₂	2.24 (0.15)	2.27 (0.11)	2.53 (0.05)	2.89 (0.05)
III - 0.51 mg/m ³ PbClBr	2.41 (0.05)	2.50 (0.05)	2.49 (0.04)	2.56 (0.05)
IV - 9.93 ppm SO ₂ + 0.50 mg/m ³ PbClBr	2.51 (0.08)	3.32 (0.08)	2.56 (0.08)	2.76 (0.06)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation

	Time-Weeks			
	Pre-exposure -8	4	16	68
Ph	N.S.	SIG	SIG	N.S.
SO ₂	N.S.	N.S.	SIG	N.S.
Interaction	N.S.	SIG	SIG	N.S.

Table 27 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for total sodium (Na - mEq/liter) for male and female monkeys in Statistical Grouping C.

Groups	Time-Weeks			
	Pre-exposure -8	4	16	68
I - Control	148.0 (0.5)	143.7 (0.3)	139.2 (0.6)	145.8 (0.8)
II - 9.70 ppm SO ₂	150.4 (0.8)	141.0 (0.7)	140.9 (0.4)	145.0 (0.4)
III - 0.51 mg/m ³ PbClBr	147.1 (0.4)	145.0 (0.6)	141.8 (0.5)	148.0 (0.8)
IV - 9.93 ppm SO ₂ + 0.50 mg/m ³ PbClBr	140.5 (0.6)	145.2 (0.9)	141.8 (0.5)	148.0 (0.7)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks			
	Pre-exposure -8	4	16	68
Pb	SIG	SIG	SIG	SIG
SO ₂	SIG	N.S.	N.S.	N.S.
Interaction	SIG	N.S.	N.S.	N.S.

Table 28 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for total serum potassium (K-mEq/liter) for male and female monkeys in Statistical Grouping C.

Groups	Time-Weeks			
	Pre-exposure -8	4	16	68
I - Control	3.75 (0.24)	3.67 (0.20)	3.64 (0.21)	4.02 (0.10)
II - 9.70 ppm SO ₂	4.02 (0.24)	4.10 (0.21)	4.48 (0.40)	4.01 (0.07)
III - 0.51 mg/m ³ PbClBr	3.62 (0.09)	3.76 (0.24)	3.86 (0.18)	3.86 (0.15)
IV - 9.93 ppm SO ₂ + 0.50 mg/m ³ PbClBr	4.41 (0.22)	4.26 (0.12)	3.69 (0.05)	4.04 (0.24)

Comparison of Experimental Treatment Effects ($p < .05$)

Source of Variation	Time Weeks			
	Pre-exposure -8	4	16	68
Pb	N.S.	N.S.	N.S.	N.S.
SO ₂	SIG	SIG	N.S.	N.S.
Interaction	N.S.	N.S.	N.S.	N.S.

Table 29 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for total serum chlorides (Cl - mEq/liter) for male and female monkeys in Statistical Grouping C.

Groups	Time-Weeks			
	Pre-exposure -8	4	16	68
I - Control	112.0 (1.1)	109.7 (0.6)	108.4 (1.0)	110.2 (0.8)
II - 9.70 ppm SO ₂	112.7 (0.6)	111.0 (0.6)	104.0 (0.4)	107.5 (0.5)
III - 0.51 mg/m ³ PbClBr	112.9 (0.5)	103.2 (0.4)	109.9 (0.6)	111.5 (0.8)
IV - 9.93 ppm SO ₂ + 0.50 mg/m ³ PbClBr	101.2 (1.1)	106.5 (0.4)	109.0 (0.6)	110.4 (0.8)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks			
	Pre-exposure -8	4	16	68
Pb	SIG	SIG	SIG	SIG
SO ₂	SIG	SIG	SIG	N.S.
Interaction	SIG	N.S.	SIG	N.S.

Table 30 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for total serum carbon dioxide (CO_2 - mEq/liter) for male and female monkeys in Statistical Grouping C.

Groups	Time-Weeks			
	Pre-exposure -8	4	16	68
I - Control	24.8 (1.0)	24.3 (0.8)	28.9 (0.7)	25.8 (0.6)
II - 9.70 ppm SO_2	27.3 (0.4)	28.2 (0.4)	28.5 (0.4)	28.2 (0.5)
III - 0.51 mg/ m^3 PbClBr	26.7 (0.6)	25.7 (0.9)	22.9 (1.7)	24.6 (1.4)
IV - 9.93 ppm SO_2 + 0.50 mg/ m^3 PbClBr	28.2 (1.1)	22.5 (0.5)	23.4 (0.7)	25.6 (0.7)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks			
	Pre-exposure -8	4	16	68
Pb	N.S.	SIG	SIG	N.S.
SO_2	SIG	N.S.	N.S.	SIG
Interaction	N.S.	SIG	N.S.	N.S.

Table 31 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for total serum calcium (Ca - mg percent) for male and female monkeys in Statistical Grouping C.

Groups	Time-Weeks				
	Pre-exposure -8	4	16	68	104
I - Control	9.47 (0.22)	9.36 (0.11)	10.16 (0.08)	9.55 (0.30)	9.88 (0.12)
II - 9.70 ppm SO ₂	9.52 (0.18)	9.12 (0.10)	9.63 (0.11)	9.97 (0.10)	9.97 (0.09)
III - 0.51 mg/m ³ PbClBr	9.77 (0.13)	9.32 (0.11)	9.35 (0.22)	9.90 (0.12)	10.02 (0.16)
IV - 9.93 ppm SO ₂ + 0.50 mg/m ³ PbClBr	9.43 (0.10)	8.89 (0.11)	9.78 (0.24)	9.74 (0.15)	9.57 (0.15)

Comparison of Experimental Treatment Effects ($p < .05$)

Source of Variation

	Time-Weeks				
	Pre-exposure -8	4	16	68	104
Pb	N.S.	N.S.	N.S.	N.S.	N.S.
SO ₂	N.S.	SIG	N.S.	N.S.	N.S.
Interaction	N.S.	N.S.	SIG	N.S.	N.S.

Table 32 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for total serum glutamic oxaloacetic transaminase (SGOT - K units) for male and female monkeys in Statistical Grouping C.

Groups	Pre-exposure	Time-Weeks			
		-8	4	16	68
I - Control	26.0 (4.8)	45.4 (3.1)	20.2 (0.8)	97.3 (21.3)	47.0 (6.2)
II - 9.70 ppm SO ₂	36.8 (4.5)	32.3 (3.3)	35.8 (6.4)	38.3 (4.7)	22.4 (1.2)
III - 0.51 mg/m ³ PbClBr	30.2 (2.1)	31.6 (2.2)	57.0 (10.7)	53.3 (4.5)	44.6 (5.4)
IV - 9.93 ppm SO ₂ + 0.50 mg/m ³ PbClBr	29.2 (2.0)	43.8 (3.9)	73.5 (15.2)	104.4 (23.5)	56.4 (3.0)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Pre-exposure	Time-Weeks			
		-8	4	16	68
Pb	N.S.	N.S.	SIG	N.S.	SIG
SO ₂	N.S.	N.S.	N.S.	N.S.	N.S.
Interaction	N.S.	SIG	N.S.	SIG	SIG

Table 33 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for total serum glutamic pyruvic transaminase (SGPT - RF units) for male and female monkeys in Statistical Grouping C.

Groups	Time-Weeks			
	Pre-exposure -8	4	16	68
I - Control	15.4 (2.8)	20.7 (3.0)	25.1 (2.7)	41.4 (2.8)
II - 9.70 ppm SO ₂	27.2 (9.2)	33.1 (6.0)	23.9 (1.4)	39.0 (1.4)
III - 0.51 mg/m ³ PbClBr	26.3 (2.5)	27.7 (1.5)	20.2 (3.0)	47.4 (0.7)
IV - 9.93 ppm SO ₂ + 0.50 mg/m ³ PbClBr	33.5 (1.6)	30.4 (2.1)	31.4 (2.5)	33.9 (3.1)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks			
	Pre-exposure -8	4	16	68
Pb	N.S.	N.S.	N.S.	N.S.
SO ₂	N.S.	SIG	N.S.	SIG
Interaction	N.S.	N.S.	SIG	SIG

Table 34 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for total lactic acid dehydrogenase (LDH - WROB units) for male and female monkeys in Statistical Grouping C.

Groups	Time-Weeks			
	Pre-exposure -8	4	16	68
I - Control	512 (99)	746 (48)	572 (80)	1573 (156)
II - 9.70 ppm SO ₂	1088 (302)	757 (85)	826 (113)	799 (81)
III - 0.51 mg/m ³ PbClBr	926 (56)	794 (82)	822 (173)	1306 (129)
IV - 9.93 ppm SO ₂ + 0.50 mg/m ³ PbClBr	787 (63)	824 (76)	1102 (187)	1342 (144)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks			
	Pre-exposure -8	4	16	68
Pb	N.S.	N.S.	N.S.	N.S.
SO ₂	N.S.	N.S.	N.S.	N.S.
Interaction	SIG	N.S.	N.S.	SIG

Table 35 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for total alkaline phosphatase (Alk. PO₄ - KA units) for male and female monkeys in Statistical Grouping C.

Groups	Pre-exposure -8	Time-Weeks			
		4	16	68	104
I - Control	57.2 (17.3)	58.6 (8.8)	55.3 (8.3)	41.9 (7.3)	48.4 (8.6)
II - 9.70 ppm SO ₂	91.6 (48.3)	40.0 (4.1)	50.5 (9.7)	53.8 (8.1)	41.2 (7.2)
III - 0.51 mg/m ³ PbClBr	54.4 (8.6)	50.7 (6.9)	67.5 (9.9)	49.2 (8.4)	41.4 (7.6)
IV - 9.93 ppm SO ₂ + 0.50 mg/m ³ PbClBr	41.4 (4.2)	52.0 (11.2)	61.1 (9.1)	55.9 (9.0)	49.9 (11.2)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Pre-exposure -8	Time-Weeks			
		4	16	68	104
Pb	N.S.	N.S.	N.S.	N.S.	N.S.
SO ₂	N.S.	N.S.	N.S.	N.S.	N.S.
Interaction	N.S.	N.S.	N.S.	N.S.	N.S.

Table 36 - Mean values $\pm$ (S.E.) for blood gas and pH variables measured in male and female monkeys in Statistical Grouping C, comprised of the following: Group I - Control, Group II - 9.70 ppm SO₂, Group III - 0.51 mg/m³ PbClBr, and Group IV - 9.93 ppm SO₂ + 0.50 mg/m³ PbClBr.

Interval Week	PO ₂				PCO ₂				pH			
	Group I	Group II	Group III	Group IV	Group I	Group II	Group III	Group IV	Group I	Group II	Group III	Group IV
-3	91.6 (2.0)	89.5 (0.1)	87.5 (1.7)	86.9 (1.4)	39.9 (0.7)	37.6 (0.6)	41.0 (0.8)	44.2 (1.1)	7.38 (0.00)	7.39 (0.00)	-	7.37 (0.01)
1	87.8 (1.8)	83.4 (1.3)	91.9 (2.7)	85.8 (1.1)	37.2 (1.0)	40.2 (0.5)	43.8 (1.2)	45.2 (1.7)	7.37 (0.00)	7.33 (0.01)	7.35 (0.01)	7.37 (0.00)
6	87.8 (1.9)	82.1 (2.1)	88.9 (1.9)	90.4 (2.7)	44.4 (1.0)	39.7 (1.0)	37.9 (1.1)	41.1 (1.4)	-	7.39 (0.00)	7.37 (0.00)	7.36 (0.01)
13	87.5 (0.9)	87.1 (2.5)	90.5 (1.3)	85.0 (1.8)	39.8 (1.3)	38.2 (1.2)	38.2 (1.1)	43.8 (1.6)	7.37 (0.00)	7.35 (0.01)	7.37 (0.01)	7.36 (0.00)
26	89.6 (1.9)	84.5 (1.9)	84.5 (1.1)	92.2 (0.9)	40.3 (1.2)	43.7 (1.0)	38.7 (0.6)	38.7 (1.9)	7.38 (0.01)	7.38 (0.00)	7.37 (0.01)	7.39 (0.01)
39	85.8 (1.2)	85.5 (1.6)	88.4 (1.1)	88.9 (1.2)	40.4 (1.8)	34.7 (1.1)	37.4 (1.3)	37.3 (1.1)	7.38 (0.00)	7.36 (0.01)	7.35 (0.01)	7.39 (0.00)
65	86.5 (1.5)	86.7 (1.8)	86.5 (1.7)	-	46.1 (1.6)	42.0 (0.9)	47.4 (0.8)	-	7.38 (0.00)	7.41 (0.00)	7.36 (0.00)	-
78	91.6 (1.6)	94.2 (0.9)	97.7 (2.8)	95.1 (2.4)	42.2 (1.4)	46.0 (1.1)	51.9 (1.1)	41.4 (1.0)	7.35 (0.01)	7.39 (0.00)	7.34 (0.01)	7.36 (0.00)
91	98.5 (2.6)	82.5 (2.5)	94.5 (2.4)	95.9 (1.4)	51.1 (2.4)	50.4 (0.7)	49.8 (1.5)	43.3 (1.3)	7.37 (0.01)	7.35 (0.01)	7.39 (0.01)	7.39 (0.01)
104	95.4 (2.2)	87.8 (2.0)	83.7 (1.0)	90.5 (1.7)	39.7 (1.5)	46.8 (1.3)	39.1 (0.9)	41.3 (1.4)	7.36 (0.01)	7.34 (0.01)	7.34 (0.00)	7.37 (0.00)

Table 37 - Mean values $\pm$ (S.D.) and summary of single classification analysis of variance for terminal body weight (g.), organ weight (g.), and organ/body weight ratios (%) for male monkeys for Statistical Grouping C, comprised of the following:
 Group I - Control, Group II - 9.70 ppm SO₂, Group III - 0.51 mg/m³ PbClBr, and Group IV - 9.93 ppm SO₂ + 0.50 mg/m³ PbClBr.

Groups	Terminal Body Weight	Brain		Thyroid		Lung		Heart		Liver		Kidneys		Adrenals	
		wt.	ratio	wt.	ratio	wt.	ratio	wt.	ratio*	wt.	ratio	wt.	ratio	wt.*	ratio
I	4920 (1410)	73.8 (7.7)	1.57 (0.31)	0.53 (0.34)	0.010 (0.004)	27.8 (6.0)	0.58 (0.08)	16.6 (4.6)	0.34 (0.05)	88.1 (13.3)	1.86 (0.25)	18.6 (4.6)	0.38 (0.05)	0.63 (0.13)	0.013 (0.002)
II	4700 (829)	64.9 (6.5)	1.41 (0.24)	0.56 (0.11)	0.012 (0.002)	26.6 (3.2)	0.57 (0.04)	15.8 (3.2)	0.34 (0.03)	80.6 (8.3)	1.73 (0.15)	16.6 (2.4)	0.35 (0.01)	0.83 (0.03)	0.018 (0.003)
III	4720 (2252)	67.3 (3.5)	1.59 (0.45)	0.41 (0.13)	0.009 (0.003)	28.2 (9.9)	0.62 (0.07)	16.4 (7.4)	0.35 (0.01)	84.8 (26.5)	1.88 (0.27)	18.3 (7.6)	0.39 (0.05)	0.76 (0.35)	0.016 (0.003)
IV	4580 (1219)	63.4 (5.2)	1.44 (0.27)	0.51 (0.20)	0.011 (0.004)	25.5 (2.9)	0.58 (0.09)	15.3 (4.0)	0.34 (0.01)	97.6 (15.8)	2.19 (0.39)	20.8 (2.0)	0.47 (0.07)	0.85 (0.15)	0.019 (0.004)
Significant Differences (p $\leq$.05)															
I vs II	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	SIG	N.S.
I vs III	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.
I vs IV	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	SIG	SIG
II vs III	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.
II vs IV	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	SIG	SIG	N.S.	N.S.
III vs IV	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.

* The variances of these groups were heterogeneous.

Table 38 - Mean values $\pm$ (S.D.) and summary of single classification analysis of variance for terminal body weight (g.), organ weight (g.), and organ/body weight ratios (%) for female monkeys for Statistical Grouping C, comprised of the following: Group I - Control, Group II - 9.70 ppm SO₂, Group III - 0.51 mg/m³ PbClBr, and Group IV - 9.93 ppm SO₂ + 0.50 mg/m³ PbClBr.

Groups	Terminal Body Weight	Brain		Thyroid		Lung		Heart		Liver		Kidneys		Adrenals	
		wt.*	ratio	wt.	ratio	wt.	ratio	wt.	ratio	wt.	ratio*	wt.	ratio	wt.*	ratio*
I	3075 (206)	59.5 (3.1)	1.94 (0.13)	0.43 (0.09)	0.014 (0.004)	21.6 (2.4)	0.70 (0.08)	9.7 (0.8)	0.31 (0.01)	66.3 (4.4)	2.16 (0.17)	13.2 (1.4)	0.43 (0.04)	0.76 (0.29)	0.025 (0.010)
II	3325 (824)	60.9 (2.8)	1.87 (0.30)	0.60 (0.08)	0.018 (0.004)	23.6 (1.1)	0.72 (0.11)	10.2 (1.5)	0.31 (0.03)	63.7 (4.8)	1.95 (0.27)	12.7 (1.0)	0.39 (0.05)	0.58 (0.04)	0.018 (0.004)
III	2750 (342)	58.9 (6.3)	2.16 (0.32)	0.30 (0.11)	0.011 (0.004)	20.7 (2.8)	0.75 (0.05)	10.2 (2.7)	0.37 (0.05)	59.0 (9.7)	2.14 (0.14)	13.7 (1.8)	0.50 (0.05)	0.69 (0.13)	0.025 (0.002)
IV	3075 (287)	57.9 (0.9)	1.89 (0.19)	0.35 (0.11)	0.011 (0.004)	18.9 (0.7)	0.62 (0.06)	11.8 (2.7)	0.38 (0.06)	82.0 (7.7)	2.67 (0.04)	14.8 (1.2)	0.48 (0.01)	0.72 (0.09)	0.023 (0.002)
Significant Differences ($p \leq .05$)															
I vs II	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.
I vs III	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.
I vs IV	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	SIG	N.S.	N.S.	N.S.	N.S.
II vs III	N.S.	N.S.	N.S.	SIG	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	SIG	N.S.	SIG
II vs IV	N.S.	N.S.	N.S.	SIG	N.S.	SIG	N.S.	N.S.	N.S.	SIG	SIG	N.S.	N.S.	SIG	N.S.
III vs IV	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	SIG	SIG	N.S.	N.S.	N.S.	N.S.

* The variances of these groups were heterogeneous.

Table 39 - Histopathology incidence table for Statistical Grouping C,
 comprised of the following: Group I - Control, Group II - 9.70 ppm
 SO₂, Group III - 0.51 mg/m³ PbClBr, and Group IV - 9.93 ppm SO₂ +
 0.50 mg/m³ PbClBr.

	GROUPS			
	<u>I</u>	<u>II</u>	<u>III</u>	<u>IV</u>
LUNG				
Focal Pleural Thickening	2/9	2/9	2/9	1/9
Peribronchial Brown Pigment	1/9	5/9	3/9	2/9
Artifactual Emphysema	4/9	5/9	0/9	0/9
Alveolar Duct Fibrosis	9/9	3/9	2/9	2/9
Thickening Bronchiolar Wall	0/9	0/9	1/9	0/9
Bronchiolar Epithelial Hyperplasia	0/9	0/9	1/9	0/9
Bronchiolar Epithelial Hypertrophy	0/9	0/9	2/9	0/9
Pneumonocyte Hyperplasia	1/9	1/9	0/9	2/9
Peribronchial Lymphoid Hyperplasia	1/9	0/9	0/9	2/9
Emphysema	0/9	0/9	0/9	1/9
Focal Necrosis	0/9	1/9	0/9	0/9
Focal Hemorrhage	0/9	1/9	0/9	0/9
Parasite	0/9	1/9	0/9	0/9
Perivascular Edema	0/9	0/9	0/9	0/9
Pulmonary Edema	0/9	1/9	0/9	0/9
Bronchiolitis	1/9	0/9	0/9	1/9
Bronchitis	0/9	0/9	1/9	0/9
Monkey Pox	0/9	1/9	0/9	0/9
Vasculitis	1/9	0/9	0/9	0/9
Granuloma	0/9	0/9	0/9	0/9
Pneumonitis	0/9	0/9	0/9	0/9
Abscess	0/9	0/9	0/9	1/9
Lung Mite Infestation	1/9	0/9	0/9	0/9
Adenomatosis	0/9	0/9	0/9	0/9
Bronchiectasis	0/9	0/9	0/9	0/9
Purulent Pneumonia	0/9	0/9	0/9	0/9
Epithelial Necrosis	0/9	0/9	0/9	0/9
Thickened Alveolar Wall	0/9	0/9	1/9	0/9
Pleuritis	0/9	0/9	0/9	0/9
Crystallin Material (yellow)	0/9	0/9	2/9	1/9
Mucous	0/9	0/9	0/9	2/9
Focal Fibrosis	0/9	0/9	0/9	0/9
Pleural Fibrosis	0/9	0/9	0/9	0/9
Alveolar Wall Fibrosis	0/9	0/9	2/9	2/9
Vacuolated Media	0/9	0/9	0/9	0/9
Endothelial Hyperplasia	0/9	0/9	0/9	0/9
Stenotic	0/9	0/9	0/9	0/9
Chronic Pneumonia	0/9	0/9	0/9	0/9
Eroded Bronchi	0/9	0/9	0/9	0/9
Emphysematous Bulla	0/9	0/9	0/9	0/9

Table 39 - Continued

	GROUPS			
	<u>I</u>	<u>II</u>	<u>III</u>	<u>IV</u>
LUNG - Continued				
Atelectasis	0/9	0/9	0/9	0/9
Congested	0/9	0/9	0/9	0/9
Extravasated Blood	0/9	0/9	0/9	0/9
Collapsed Alveolar Wall	0/9	0/9	0/9	0/9
LIVER				
Pericholangitis	0/9	1/9	3/9	4/9
Bile Duct Proliferation	1/9	3/9	3/9	3/9
Focal Necrosis	0/9	1/9	0/9	0/9
Sinusoidal Pigment	2/9	7/9	2/9	0/9
Focal Hepatitis	0/9	0/9	0/9	0/9
Focal Lymphoid Infiltration	1/9	2/9	1/9	0/9
Nematodiasis	0/9	1/9	0/9	0/9
Thick Capsule	0/9	0/9	0/9	0/9
Granuloma	0/9	0/9	0/9	0/9
Abscess	0/9	0/9	0/9	0/9
Hepatocyte Vacuolation	0/9	0/9	1/9	1/9
Greenish Granular Material in the Hepatocytes	0/9	0/9	1/9	0/9
PERIBRONCHIAL LYMPH NODE				
Phagocytized Pigment	6/9	5/9	7/9	7/9
Lymphoid Activity	8/9	6/9	0/9	0/9
Lymphoid Atrophy	0/9	0/9	0/9	0/9
Adenitis	0/9	0/9	0/9	0/9
Granuloma	1/9	2/9	0/9	0/9
Reticuloendothelial Cell Hyperplasia	1/9	0/9	0/9	0/9
Lymphadenitis	0/9	0/9	0/9	0/9
TRACHEA				
Tracheitis	1/9	0/9	0/9	0/9
Increase in Goblet Cells	0/9	4/9	0/9	0/9
Exudate in Lumen	0/9	1/9	0/9	0/9
Necrosis of the Epithelium	0/9	1/9	0/9	0/9
Inclusion Bodies	0/9	1/9	0/9	0/9
Epithelial Hyperplasia	0/9	1/9	0/9	0/9
Cilia Atrophy	0/9	0/9	0/9	0/9
Squamous Metaplasia	0/9	0/9	0/9	0/9
Focal Hemorrhage	0/9	0/9	0/9	0/9

Table 39 - Continued

	GROUPS			
	<u>I</u>	<u>II</u>	<u>III</u>	<u>IV</u>
KIDNEY				
Interstitial Nephritis	0/9	2/9	2/9	0/9
Epithelial Vacuolation	1/9	3/9	3/9	8/9
Tubular Dilatation	3/9	2/9	0/9	1/9
Loss of the Brush Border	0/9	2/9	3/9	3/9
Nuclear Vesiculation	0/9	0/9	0/9	7/9
Tubular Hypertrophy	0/9	0/9	0/9	1/9
Pyelitis	0/9	1/9	0/9	0/9
Focal Mineralization	0/9	0/9	1/9	0/9
Glomerular Degeneration	0/9	2/9	0/9	0/9
Inclusion Bodies	0/9	0/9	7/9	8/9
Vasculitis	0/9	0/9	0/9	0/9
Congestion	0/9	0/9	0/9	0/9
Focal Fibrosis	0/9	0/9	0/9	0/9
Perirenal Abscess	0/9	0/9	0/9	1/9
Protein Inhibition	0/9	0/9	1/9	0/9
Intima Thickening	0/9	0/9	0/9	0/9
Endothelial Hyperplasia	0/9	0/9	0/9	0/9
HEART				
Focal Myocarditis	3/9	2/9	0/9	0/9
Endocarditis	0/9	0/9	0/9	0/9
Epicarditis	0/9	1/9	0/9	0/9
Myocardial Degeneration	1/9	0/9	0/9	0/9
Vasculitis	0/9	0/9	0/9	0/9
Subendocardial Hemorrhage	0/9	1/9	0/9	0/9
Thickened Endocardium	0/9	0/9	0/9	0/9
Focal Hyperplasia in the Endothelium	0/9	0/9	0/9	0/9
Intima Thickening	0/9	0/9	0/9	0/9
Granular Pigment	0/9	0/9	0/9	0/9



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VI. STATISTICAL GROUPING D - RESULTS OF THE CHRONIC EXPOSURE OF CYNOMOLGUS MONKEYS TO 65.46 PPM CARBON MONOXIDE (CO), 0.51 MG/M³ LEAD CHLOROBROMIDE (PbClBr) AND 66.43 PPM CO COMBINED WITH 0.47 MG/M³ PbClBr.

Four groups of animals comprise the fourth statistical grouping-D. One group was maintained as the control group exposed to filtered room air, while the other three groups were exposed to carbon monoxide and lead chlorobromide singly and in binary combination. Group designations used throughout this section are presented in Table 13.

Table 13 - Group D designations

<u>Group Designation (No.)</u>	<u>Agent</u>	<u>Nominal Concentration</u>	<u>Mean Analytical Concentration</u>
I (1)	Control	0	0
II (7)	CO	67.50 ppm	65.46 ppm
III (9)	PbClBr	0.60 mg/m ³	0.51 mg/m ³
IV (20)	CO	67.50 ppm	66.43 ppm
	PbClBr	0.60 mg/m ³	0.47 mg/m ³

1. Exposure Concentrations

The chamber concentrations as determined analytically are presented in Tables 1, 2, and 3, Appendix D, for Groups II, III, and IV, respectively. The mean and standard deviation for the group exposed to CO alone was 65.46 ppm $\pm$ 3.33; for the group exposed to PbClBr alone 0.51 mg/m³ $\pm$ 0.27; and for the group exposed to the combination of CO and PbClBr, the means and standard deviations were 66.43 ppm $\pm$ 2.28 and 0.47 mg/m³ $\pm$ 0.21, respectively.



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2. Particle Size Determination

The mean and geometric deviation of all count particle size determinations for PbClBr converted to mass median diameter (MMD) were $0.550\mu \pm 1.57$ and $1.050\mu \pm 1.79$ for Groups III and IV, respectively. A composite size vs. distribution log-probability plot from the pooled count data is presented in Figures 66 and 67 for Groups III and IV, respectively.

3. Biological Measurements

3.1. Body Weight

Analysis of variance of regression for body weight (Table 4, Appendix D) indicated no significant differences in slopes among the groups. The regression curves (Figure 68) indicated a trend toward increasing body weight values in all groups and growth rate was similar in all groups except Group II which started slightly heavier and ended slightly lighter due to the deaths of two male members of the group.

3.2. Survival

No deaths occurred in Groups I, III or IV during the 104 weeks of exposure. Two deaths occurred in Group II during Weeks 42 and 78 of the exposure period. Daily observation of the animals revealed no clinical signs of toxicity or abnormal behavior attributable to the exposure atmospheres.

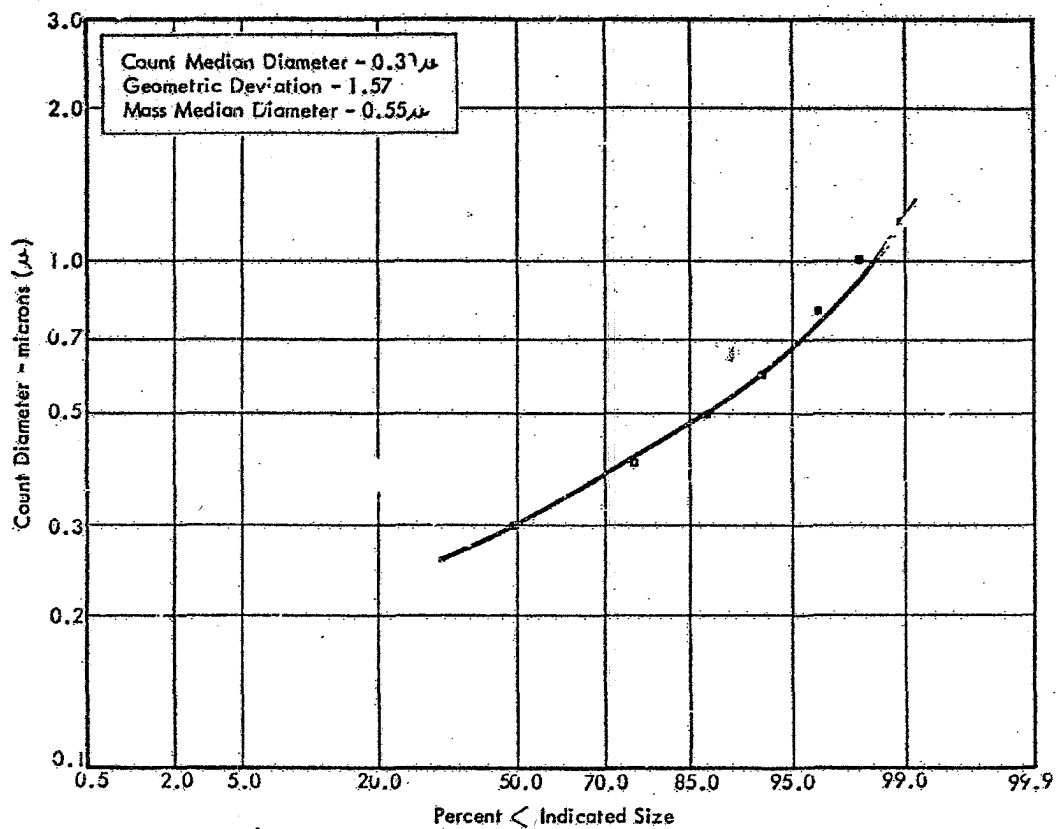


Figure 66 - Particle size distributions (count diameter) of PbClBr.

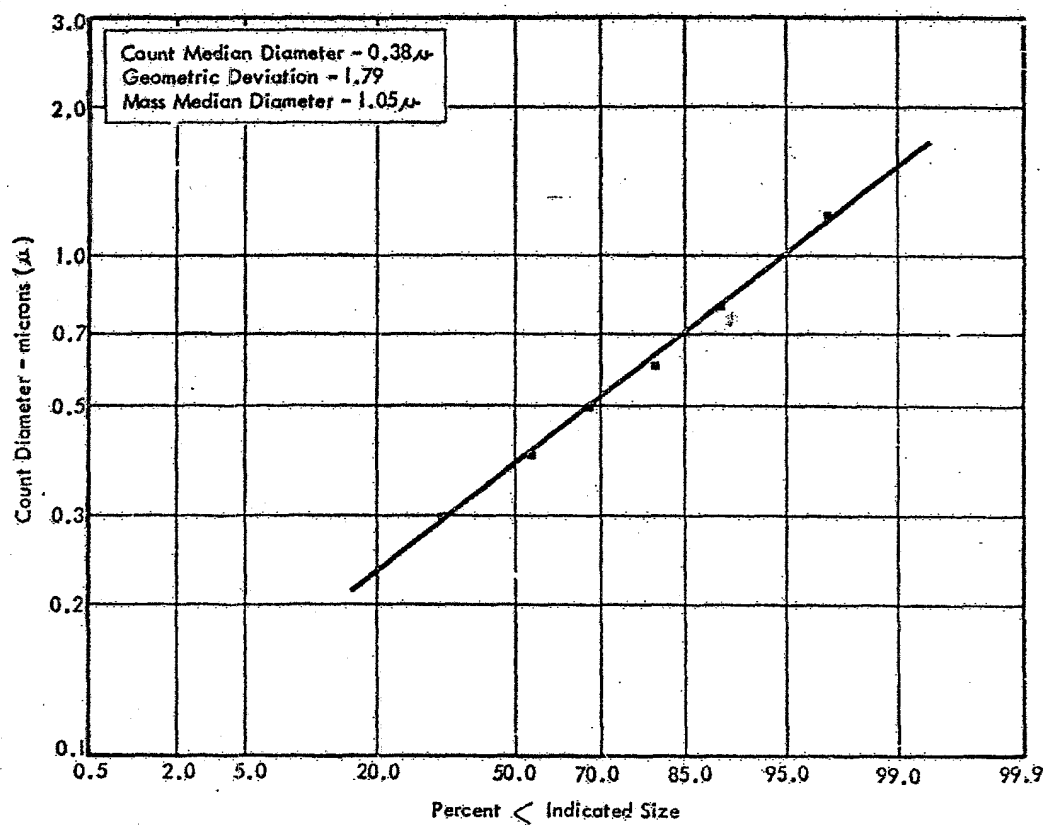


Figure 67 - Particle size distributions (count diameter) of PbClBr for the group exposed to the combination of PbClBr and CO.

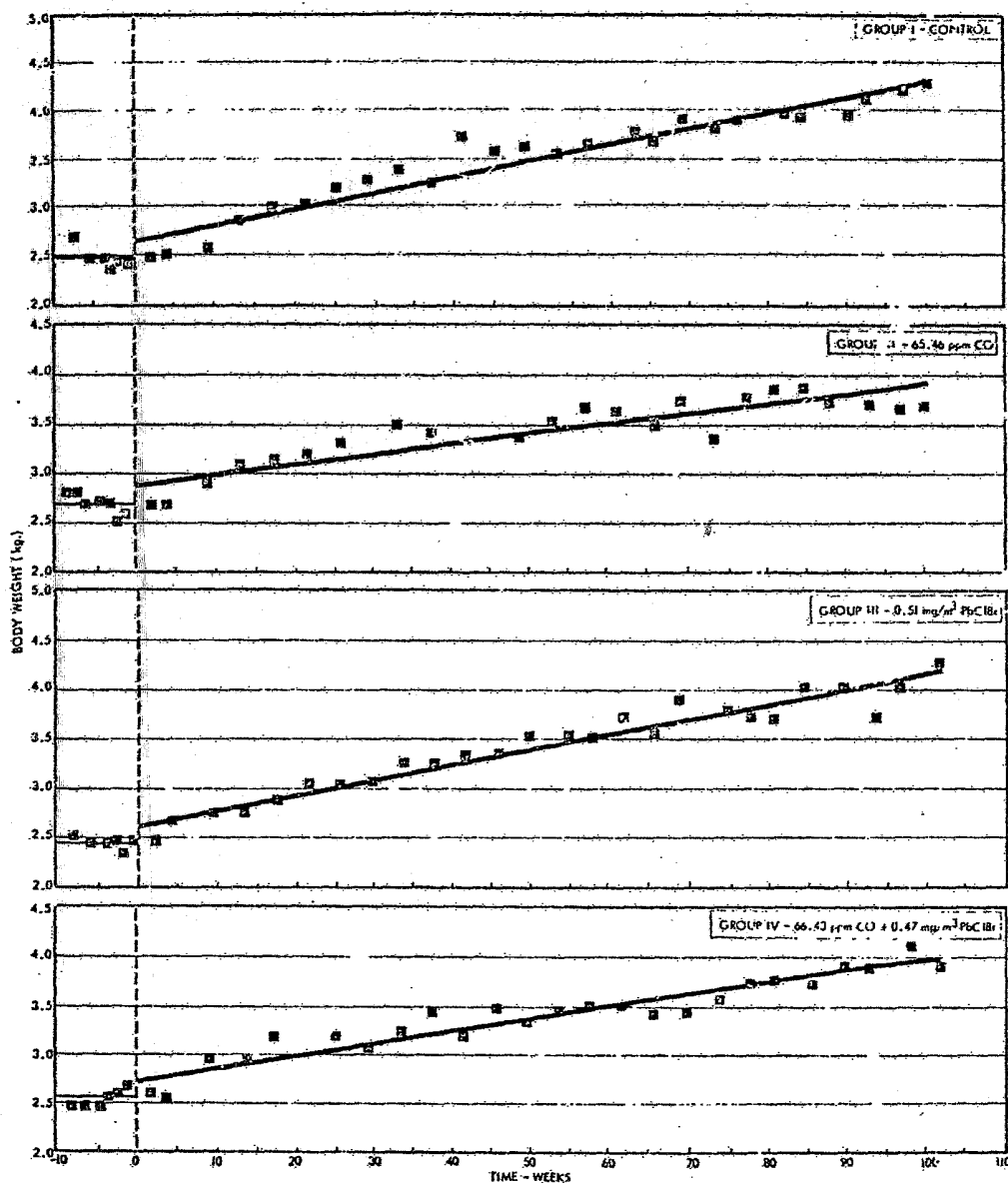


Figure 68 - First degree polynomial regression curves for body weight prior to and during exposure to carbon monoxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.



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3.3. Pulmonary Function Tests

3.3.1. Mechanical Properties of the Lung and Respiratory System

3.3.1.1. Total Respiratory System Flow Resistance During Inspiration [$R_{rs}(i)$]

Analysis of variance of regression for $R_{rs}(i)$ (Table 5, Appendix D) revealed non-parallelism among the groups. The third degree polynomial regression curves (Figure 69) indicated that $R_{rs}(i)$ values for Group I decreased slightly at the beginning of the exposure whereas values for Groups III and IV similarly increased slightly. Separate t-tests of the pre-exposure adjusted means for the first nine weeks indicated that Group I was significantly lower than Group III and Group IV during this early interval ($t = 4.33$, d.f. = 16 and $t = 4.66$, d.f. = 16, respectively).

3.3.1.2. Total Respiratory System Flow Resistance During Expiration [$R_{rs}(e)$]

Analysis of variance of regression for $R_{rs}(e)$ (Table 6, Appendix D) indicated non-parallelism among the groups. Third degree polynomial regression curves (Figure 70) indicated that Group II started into the experiment with lower $R_{rs}(e)$ values than the other groups, and did not exhibit as much of a decrease as the other groups. A t-test of pre-exposure adjusted overall exposure means comparing Groups I and II indicated that Group II was relatively significantly higher throughout the exposure period ($t = 5.03$, d.f. = 14.3). A similar test comparing Groups I and IV indicated that Group IV was relatively higher also ($t = 3.72$, d.f. = 16). Group III was not significantly different from Group I by this test ($t = 1.92$, d.f. = 16).

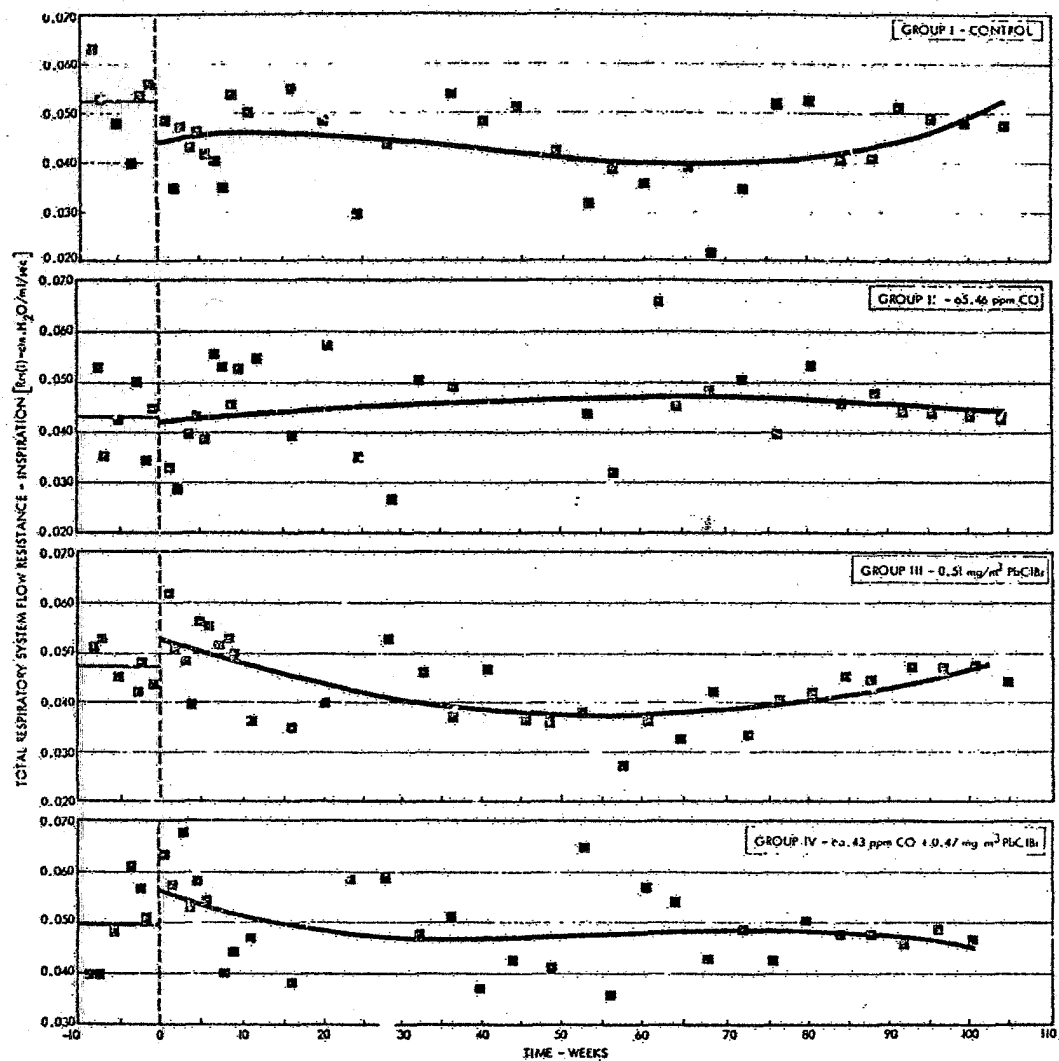


Figure 69 - Third degree polynomial regression curves for $R_{rs}(i)$ prior to and during exposure to carbon monoxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.

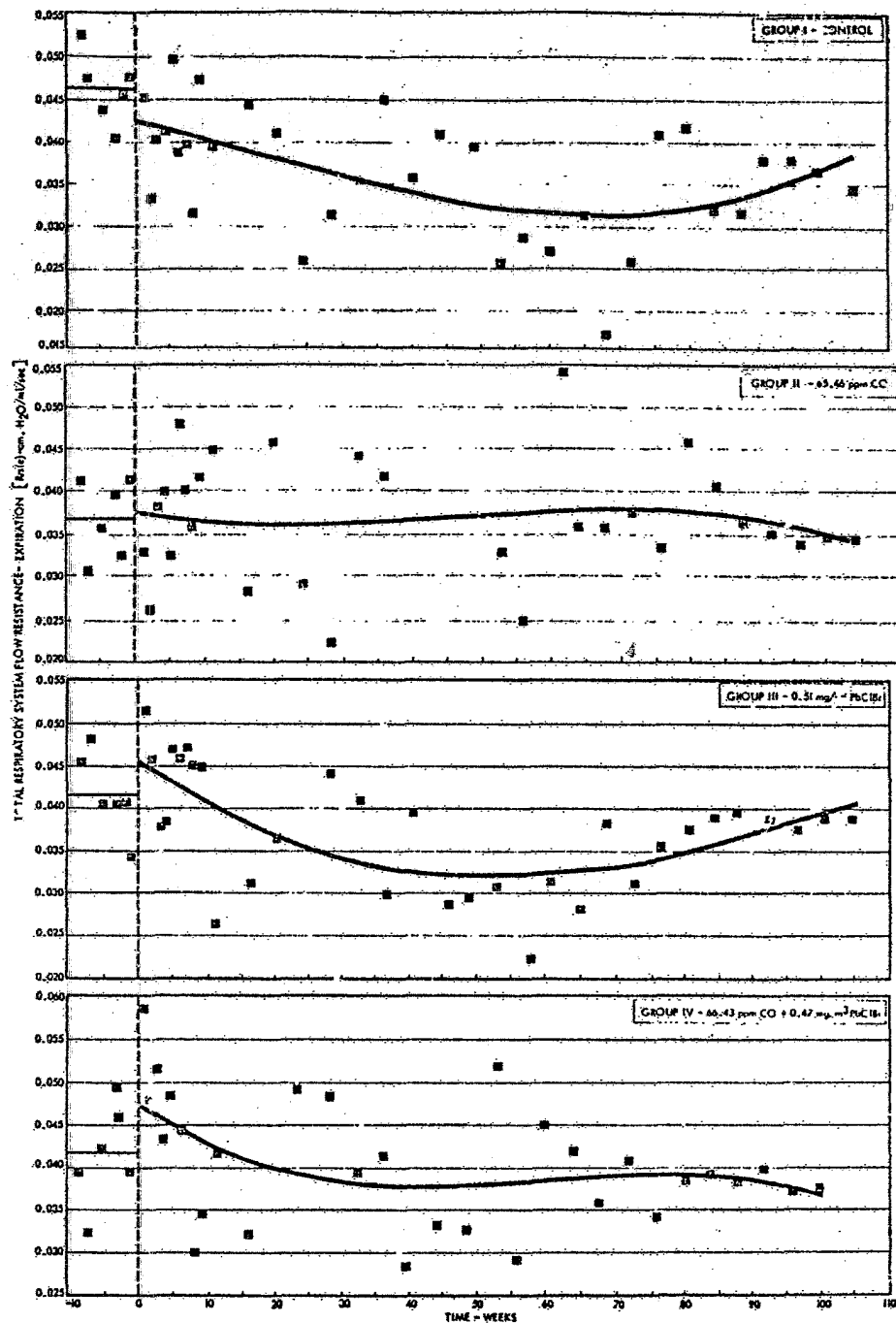


Figure 70 - Third degree polynomial regression curves for Rrs(e) prior to and during exposure to carbon monoxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.



3.3.1.3. Tidal Volume (V_T)

Analysis of variance of regression for V_T (Table 7, Appendix D) revealed no significant differences in slopes among the groups. V_T increased with time in all groups, as shown in Figure 71.

3.3.1.4. Respiratory Rate (RR)

Analysis of variance of regression for RR (Table 8, Appendix D) indicated slight non-parallelism among the groups. The third degree polynomial regression curves (Figure 72) indicated that Groups II, III, and IV exhibited essentially no change during the exposure period, while Group I demonstrated slightly decreasing values due to an abrupt increase after "exposure" started.

3.3.1.5. Dynamic Compliance of the Lung [$C_{dyn}(1)$]

Analysis of variance of regression for $C_{dyn}(1)$ (Table 9, Appendix D) revealed no significant differences in slopes among the groups. The third degree polynomial regression curves (Figure 73) indicated that all groups increased in $C_{dyn}(1)$ during the experiment, with Group I showing a sharp increase after "exposure" began. Although the pre-exposure adjusted means of the first year were significantly different between Groups I and III ($t = 2.69$, d.f. = 16), the fact that Group I showed a large increase at the start of exposure renders any interpretation difficult.

3.3.1.6. Pulmonary Flow Resistance (R1)

Analysis of variance of regression for R1 (Table 10, Appendix D) indicated non-parallelism among the groups. The third degree polynomial regression curves (Figure 74) indicated that Group I did not decrease as much as the other groups during the exposure period. During the first nine weeks

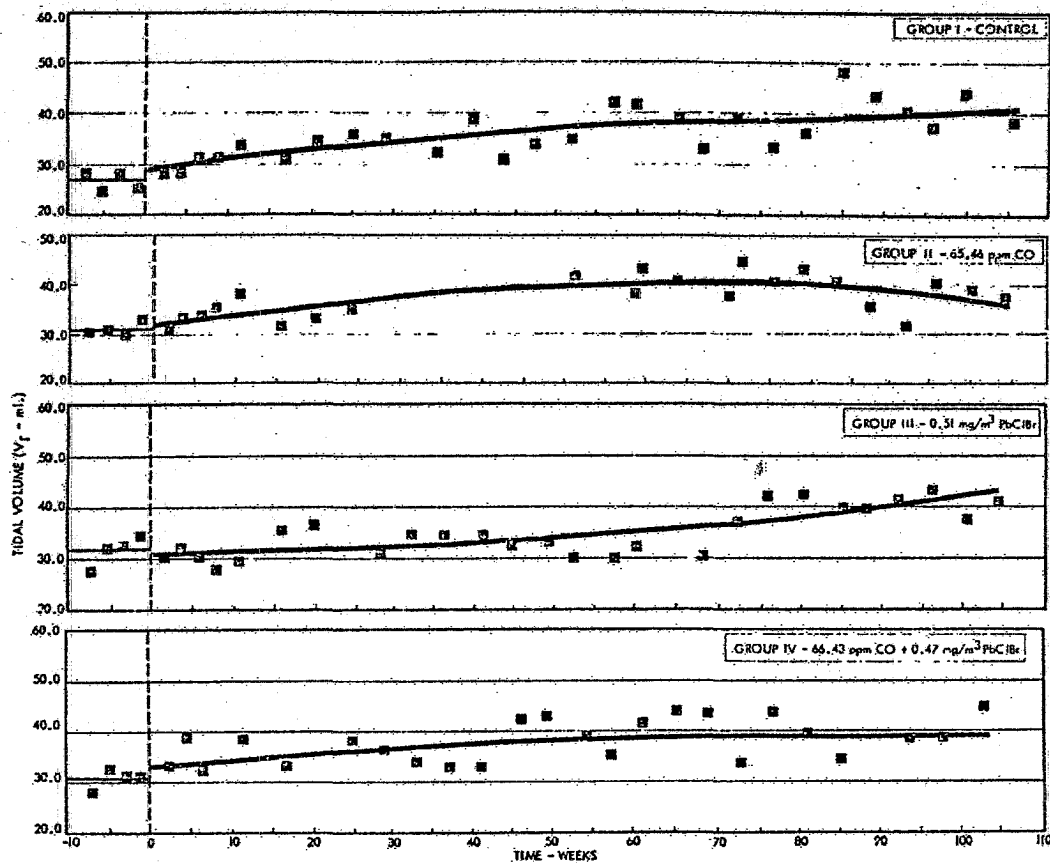


Figure 71 - Third degree polynomial regression curves for V_T prior to and during exposure to carbon monoxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.

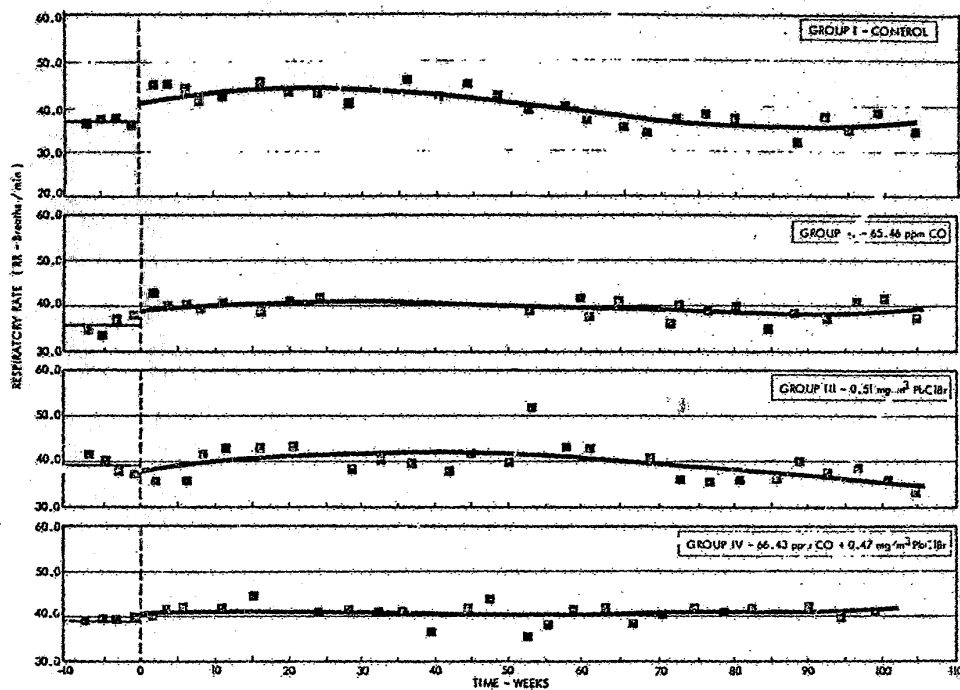


Figure 72 - Third degree polynomial regression curves for RR prior to and during exposure to carbon monoxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.

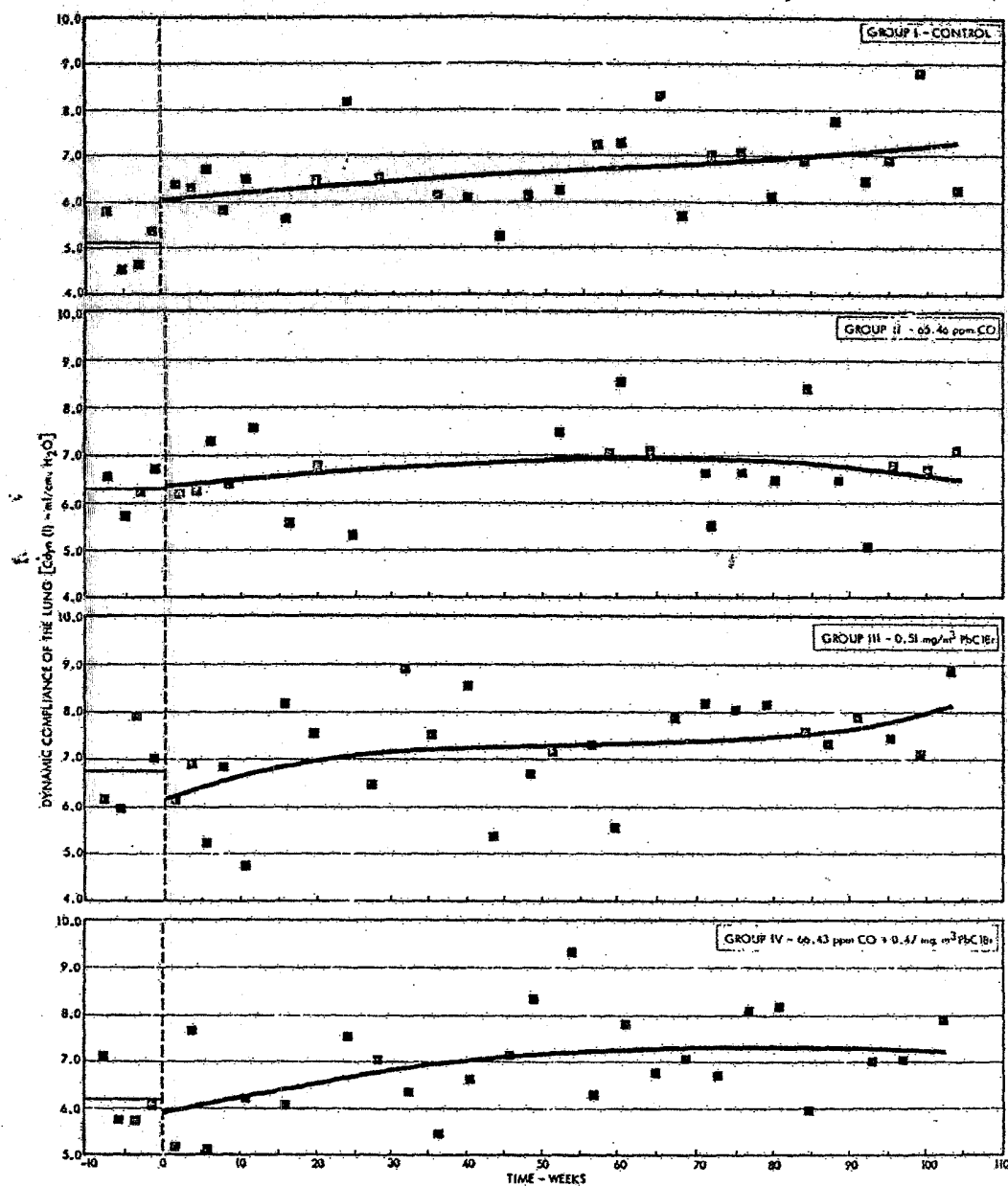


Figure 73 - Third degree polynomial regression curves for Cdyn(I) prior to and during exposure to carbon monoxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.

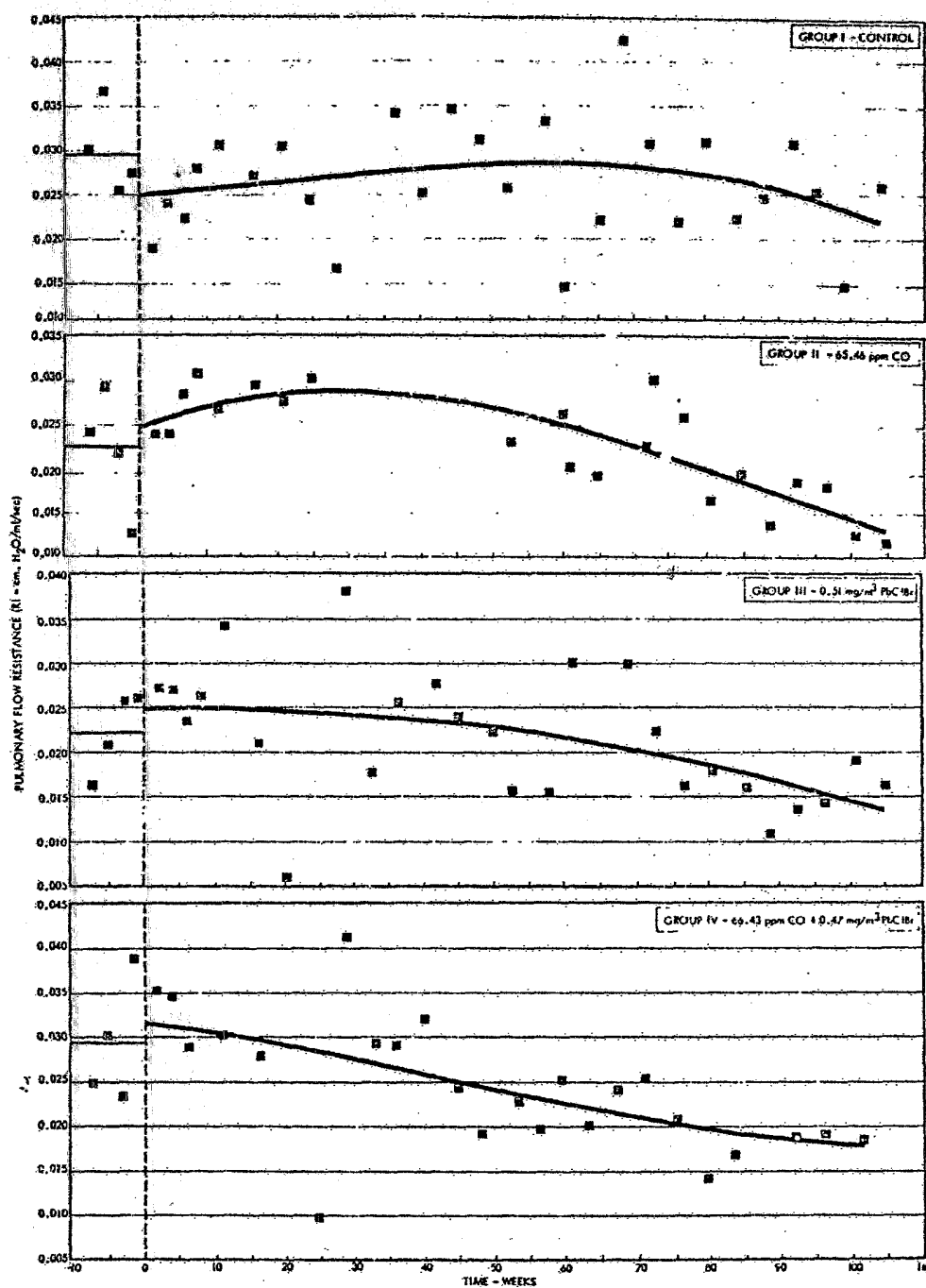


Figure 74 - Third degree polynomial regression curves for Rl prior to and during exposure to carbon monoxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.



of exposure, Group IV was significantly higher than Group I ($t = 4.66$, d.f. = 16) as was Group III ($t = 2.66$, d.f. = 16). Separate t-tests of the pre-exposure adjusted means of the overall exposure period and of the first 52 weeks exposure between Groups I and II were not significant ($t < 1.64$, d.f. = 16 and $t = 2.05$, d.f. = 16, respectively).

3.3.1.7. Work of Breathing During Inspiration per ml Tidal Volume [$W(i)/ml V_T$]

Analysis of variance of regression for $W(i)/ml V_T$ (Table 11, Appendix D) revealed no significant differences in slopes among the groups. The third degree polynomial regression curves (Figure 75) indicated that Groups III and IV were lower than Group I throughout the exposure period.

3.3.1.8. Work of Breathing During Expiration per ml Tidal Volume [$W(e)/ml V_T$]

Analysis of variance of regression for $W(e)/ml V_T$ (Table 12, Appendix D) indicated no significant differences in slopes among the groups. The third degree polynomial regression curves (Figure 76) indicated very little change in $W(e)/ml V_T$ values throughout the exposure.

3.3.2. Diffusing Capacity of the Lung for Carbon Monoxide (DL_{CO})

Analysis of variance of linear regression for DL_{CO} (Table 13, Appendix D) indicated that there were no significant differences in slopes between the groups. The third degree polynomial regression curves (Figure 77) indicated that all groups increased in DL_{CO} values with time.

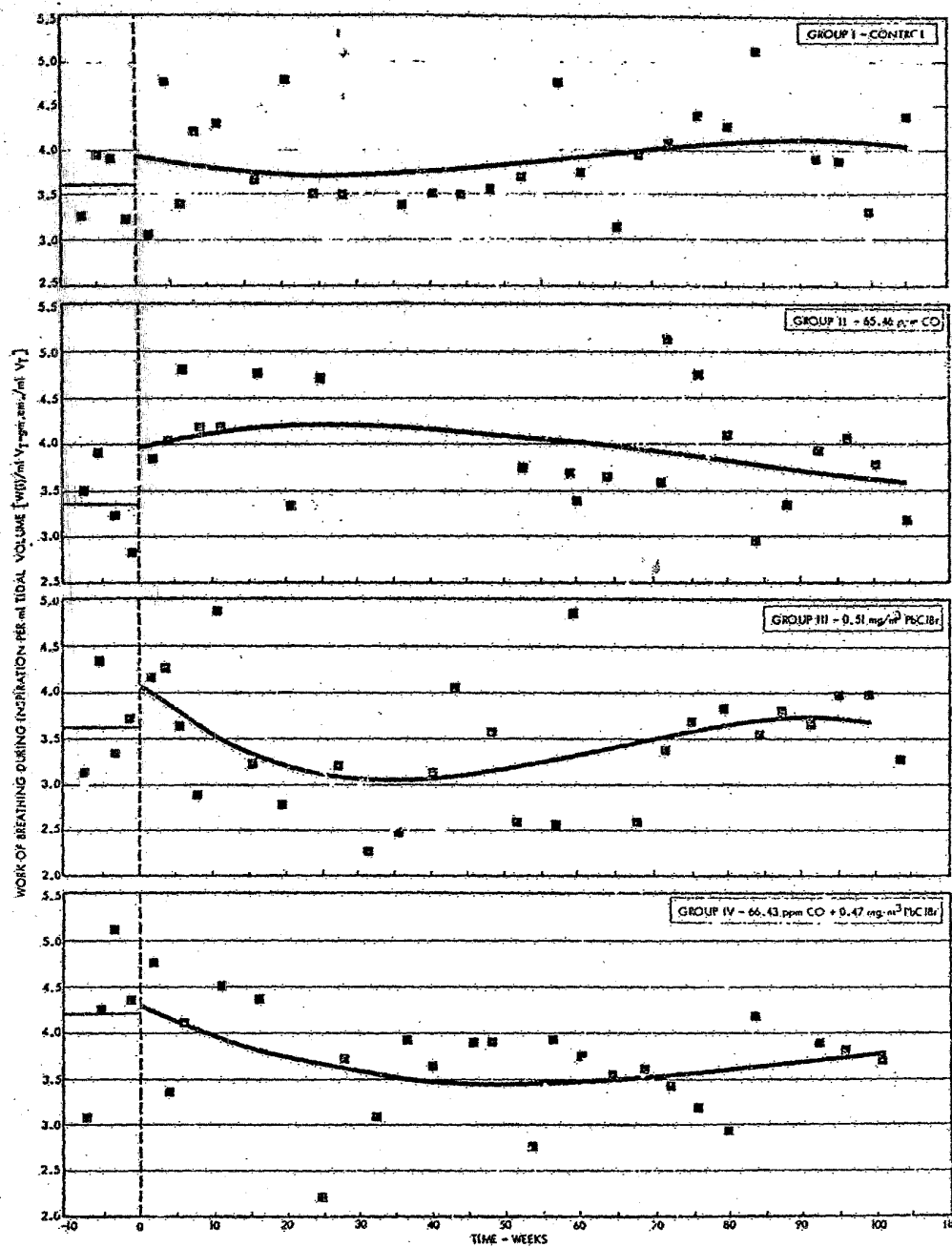


Figure 75 - Third degree polynomial regression curves for $W(i)/ml V_T$ prior to and during exposure to carbon monoxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.

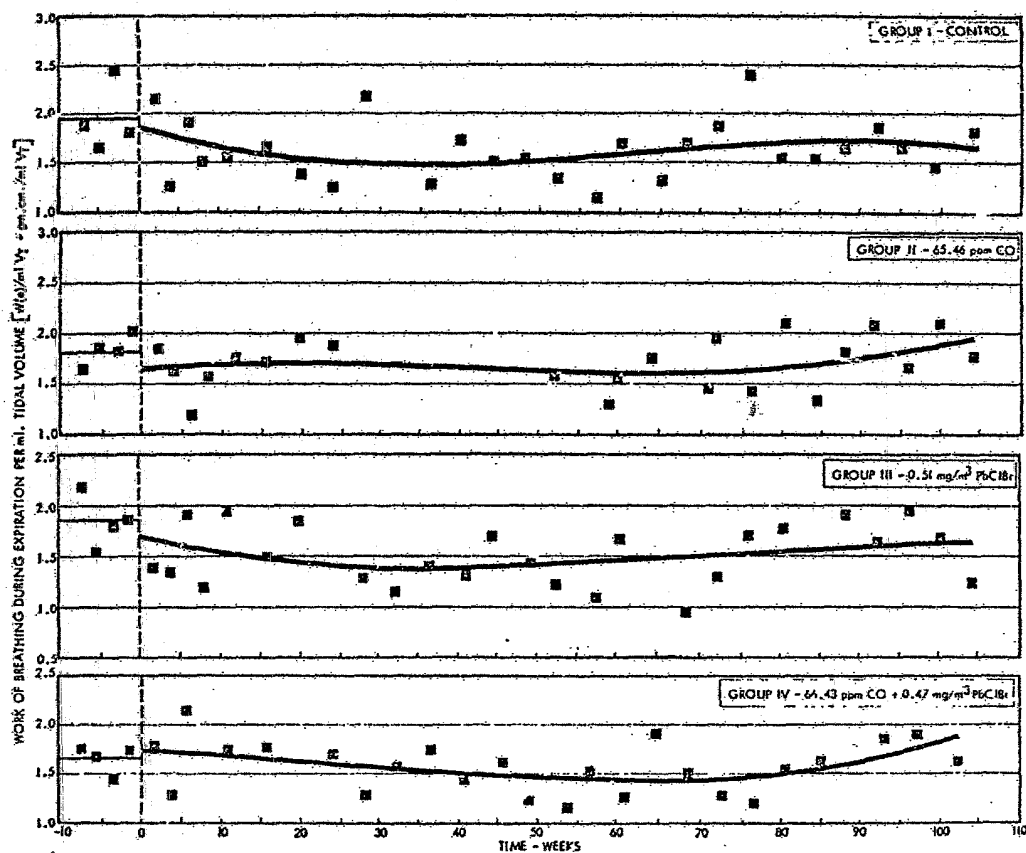


Figure 76 - Third degree polynomial regression curves for $W(e)/ml V_t$ prior to and during exposure to carbon monoxide and lead chlorobromide singly and binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.

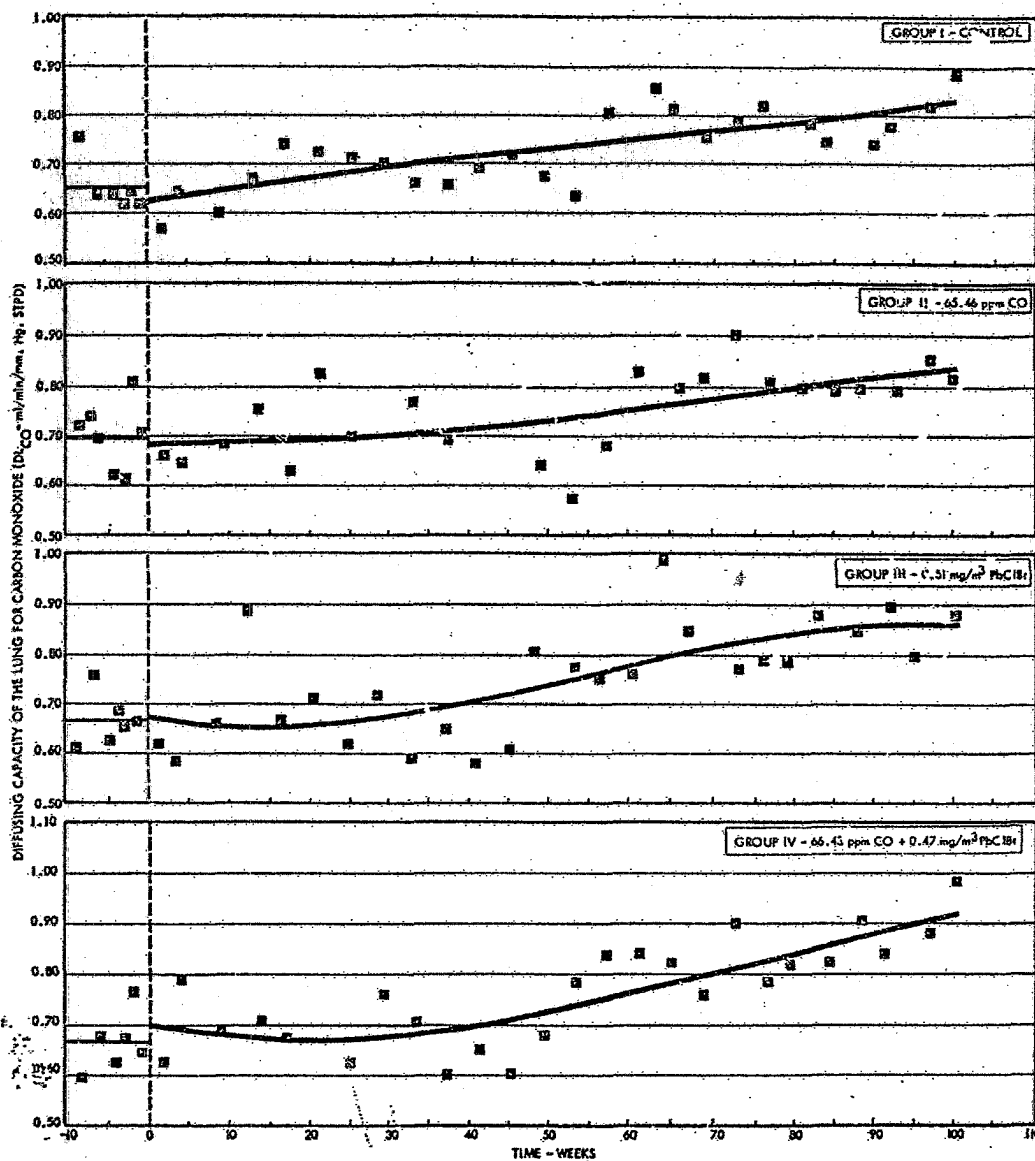


Figure 77 - Third degree polynomial regression curves for DL_{CO} prior to and during exposure to carbon monoxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.



3.3.3. Distribution of Inspired Air, Nitrogen Washout

3.3.3.1. Number of Breaths from 80% to 1% Nitrogen [$N(1\% N_2)$]

Analysis of variance of regression for $N(1\% N_2)$ (Table 14, Appendix D) indicated non-parallelism among the groups. The third degree polynomial regression curves (Figure 78) indicated that values for Group I were somewhat higher during the pre-exposure control period than values for Group II, III, and IV. During the entire exposure period, $N(1\% N_2)$ values for Groups III and IV were at a higher level than Group I values. A t-test of the pre-exposure adjusted overall exposure means of these two groups indicated that Group III was significantly higher than Group I during the exposure period ($t = 4.55$, d.f. = 16). A similar t-test comparing Groups I and IV showed a similar relationship ($t = 5.24$, d.f. = 16). A t-test of the pre-exposure adjusted overall exposure means of Groups I and II showed them to be significantly different ($t = 2.21$, d.f. = 16).

3.3.3.2. Respiratory Rate Measured During Pure Oxygen Breathing (RR')

Analysis of variance of regression for RR' (Table 15, Appendix D) indicated no significant differences in slopes among the groups. The third degree polynomial curves (Figure 79) indicated that Groups II, III, and IV were slightly higher than Group I after the 45th week. Separate t-tests of the pre-exposure adjusted overall exposure means comparing Group I to each of the experimental groups, indicated that the first two groups were relatively higher than Group I throughout exposure ($t = 2.18$, d.f. = 16; $t = 2.61$, d.f. = 16, and $t < 1.64$, d.f. = 16, respectively).

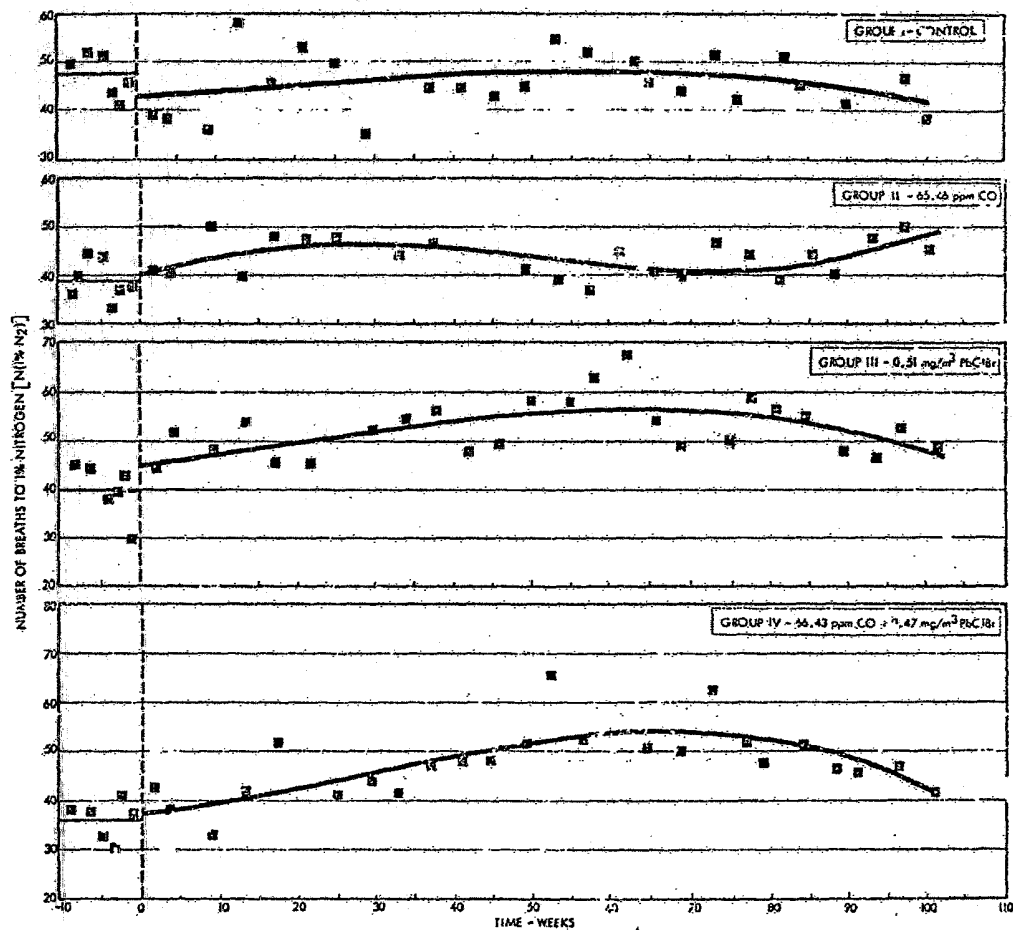


Figure 78 - Third degree polynomial regression curves for N(1% N₂) prior to and during exposure to carbon monoxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.

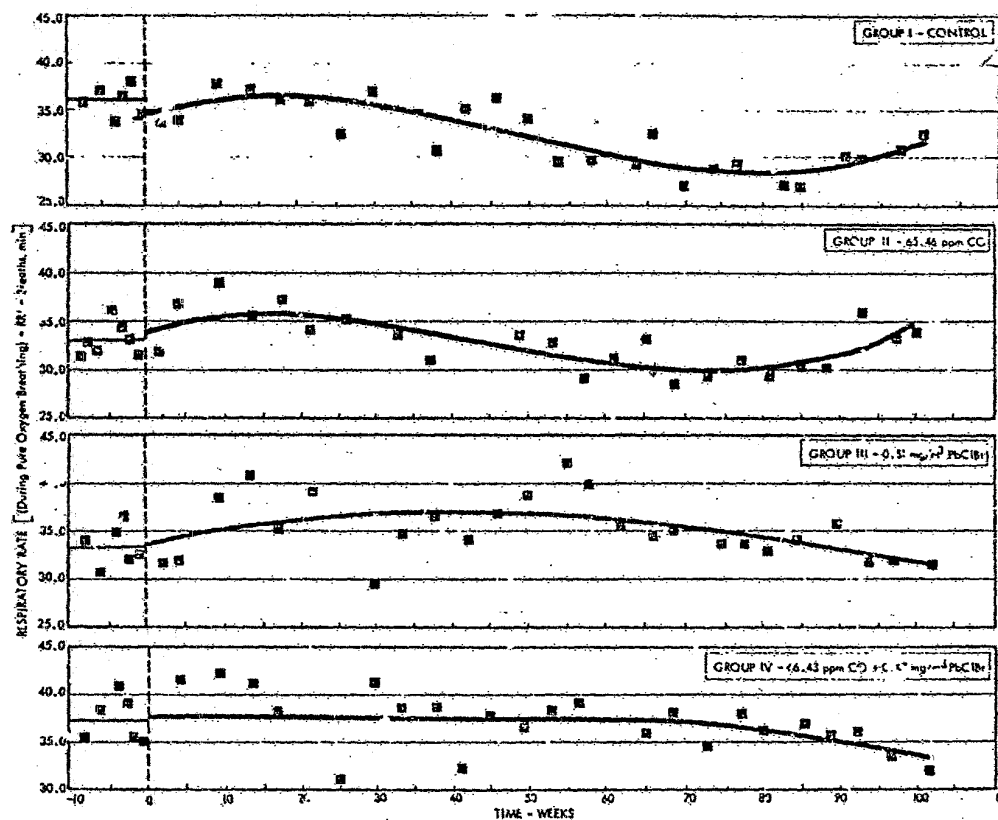


Figure 79 - Third degree polynomial regression curves for RR' prior to and during exposure to carbon monoxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.



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3.3.3.3. Cumulative Tidal Volume from 80% to 1% Nitrogen [$CV_T(1\% N_2)$]

Analysis of variance of regression for $CV_T(1\% N_2)$ (Table 16, Appendix D) indicated non-parallelism among the groups. The third degree polynomial regression curves (Figure 80) indicated that Group III was slightly higher overall than Group I throughout exposure. A t-test of the pre-exposure adjusted overall exposure means comparing these two groups indicated that Group III was significantly higher ($t = 2.24$, d.f. = 13.7) throughout the exposure period.

3.3.3.4. Tidal Volume Measured During Oxygen Breathing (V_T')

Analysis of variance of regression for V_T' (Table 17, Appendix D) revealed non-parallelism among the groups. The third degree polynomial regression curves (Figure 81) indicated that Group I had lower V_T' values than the other groups during the pre-exposure period and exhibited more of an increase during the exposure period. The lack of increase in Group II, when compared to Group I ($t = 2.51$, d.f. = 16), was probably due to the deaths of two males during the exposure period.

3.4. Hematology

The group means and analysis of variances of the various hematological variables measured are presented in Tables 18, 19, 20, and 21, Appendix D. No consistent trends were noted in any of these variables which remained within normal limits throughout. Random statistically significant differences were seen, but were not consistently related to the exposure conditions.

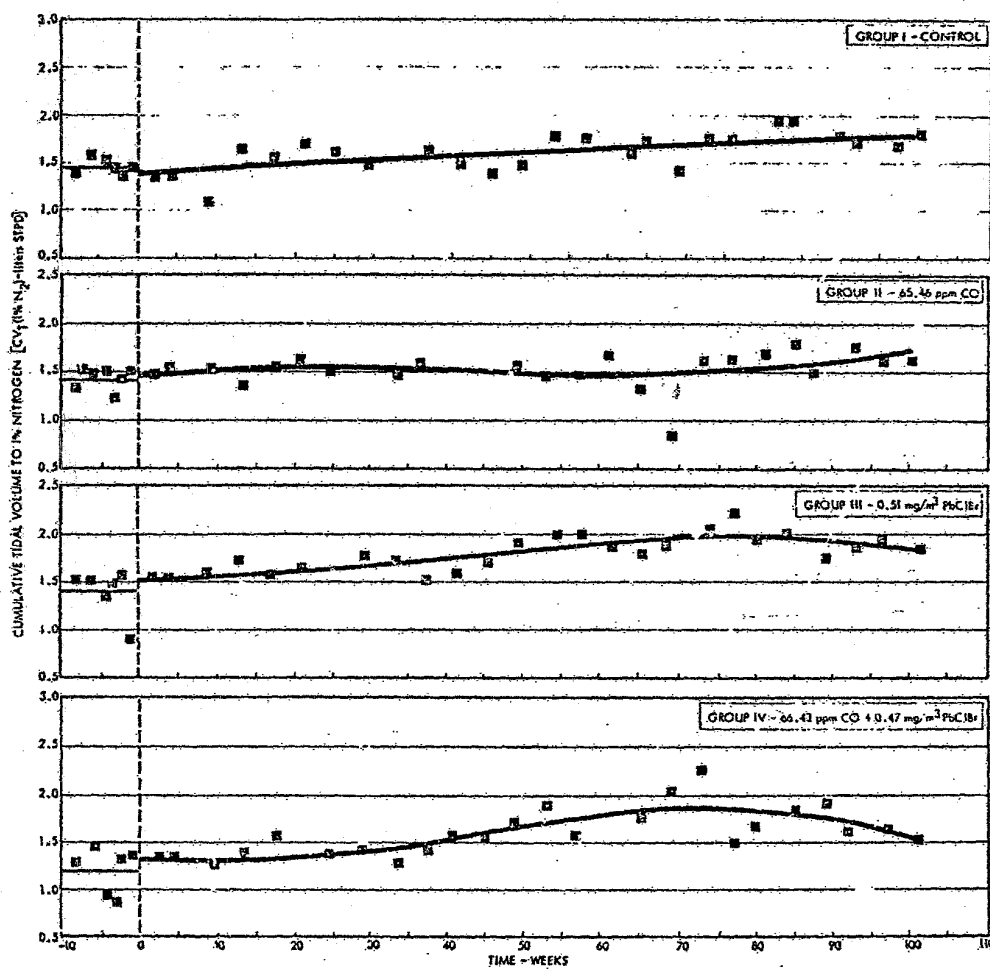


Figure 80 - Third degree polynomial regression curves for CV_T(1% N₂) prior to and during exposure to carbon monoxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.

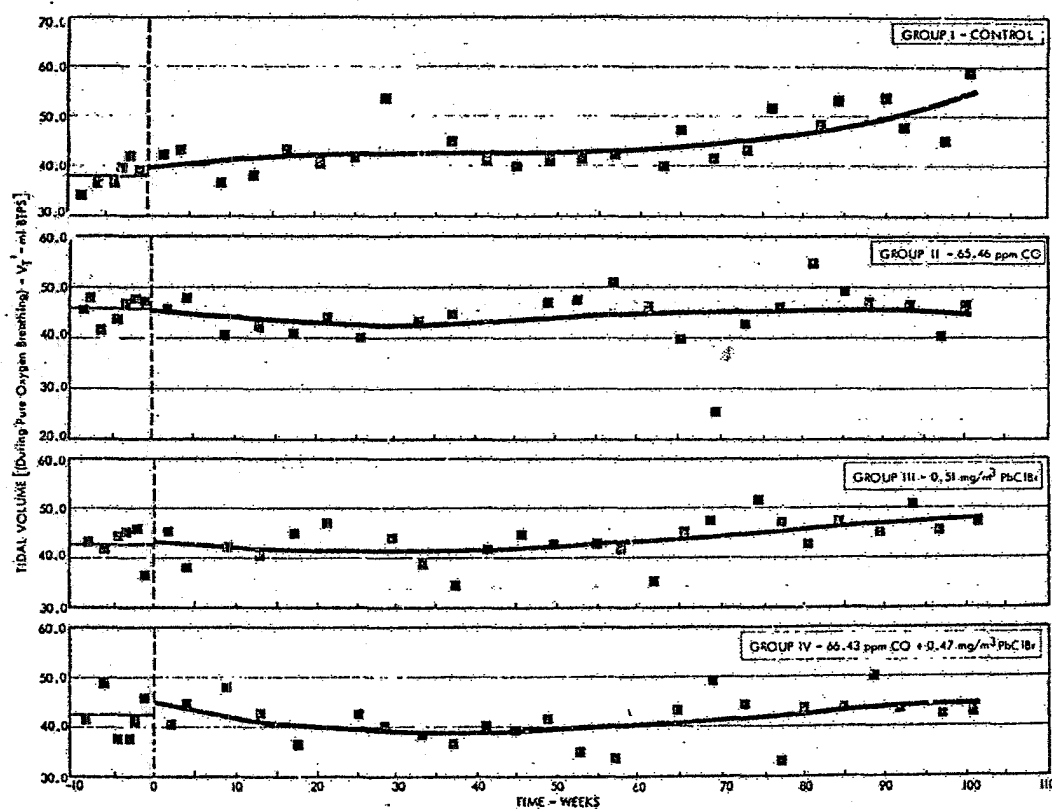


Figure 81 - Third degree polynomial regression curves for V_T' prior to and during exposure to carbon monoxide and lead chlorobromide singly and in binary combination. Each point represents the mean for the animals tested at the indicated time for the various groups.



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3.5. Clinical Biochemistry

The group means, standard errors, and the results of the analysis of variance of the various clinical biochemical variables measured are presented in Tables 22 through 35, Appendix D. Scattered statistically significant differences were noted; however, no trends were seen in any of the variables. Throughout the study, the group mean values fluctuated within the normal ranges of these variables.

3.6. Arterial Blood Gas and pH

The group means and standard errors for the blood gas variables are presented in Table 36, Appendix D. Examination of these data did not reveal any consistent trend with time. No apparent exposure-related changes were seen in any of these variables.

3.7. Terminal Body Weight, Organ Weight, and Organ Weight as a Percentage of Body Weight

The data of the terminal body weight, organ weight, and organ/body weight ratios are presented in Tables 37 and 38, Appendix D, for males and females, respectively. Single classification analysis of variance revealed that the brain weight for the males in Group IV was significantly higher than for Group I males. The mean terminal body weight for the females in Group II was higher than the terminal body weight for Group III females. The kidney weight to body weight ratio was higher in Group III females than in Group II females and the heart weight for Group II females was significantly higher than Group I females.



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3.8. Histopathology Summary

A detailed listing of the microscopic alterations seen in the lungs, tracheas, livers, kidneys, peribronchial lymph nodes, and hearts from the animals in the control and exposure groups are found in Table 39, Appendix D. Exposure-related microscopic alterations were seen in the kidneys of the animals exposed to 0.6 mg/m^3 of PbClBr . These microscopic alterations were characterized by varying degrees of degeneration of the proximal convoluted tubules. The epithelial cells of the proximal convoluted tubules were slightly vacuolated in some animals and a slight to moderate degree of nuclear vesiculation was present in some animals. Acid fast intranuclear inclusion bodies were seen in seven of the nine animals exposed to 0.6 mg/m^3 of PbClBr alone and in five of the nine animals exposed to the combination of 67.5 ppm CO and 0.6 mg/m^3 of PbClBr .

Incidental lesions not related to the exposure conditions were seen in the lungs, peribronchial lymph nodes, tracheas, hearts, and livers from the animals in both the control and exposed groups.

Animal No. 157L in the group exposed to 67.5 ppm CO died during the 42nd week of exposure. Microscopic examination of the tissues from this animal revealed lesions consistent with a diagnosis of monkey pox. Necrosis and hemorrhage were seen in the lungs and liver from this animal. Numerous inclusion bodies were present in the epithelial cells of the trachea.



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3.9. Summary

The inhalation exposure of male and female cynomolgus monkeys to 65.46 ppm CO, 0.51 mg/m³ PbClBr, and the combination of 66.43 ppm CO plus 0.47 mg/m³ PbClBr resulted in a deterioration in the distribution of ventilation in the animals in the two groups containing PbClBr. The number of breaths to 1% nitrogen measured during pure oxygen breathing was significantly elevated in the animals in both groups exposed to PbClBr. Cumulative tidal volume to 1% nitrogen and respiratory rate measured during pure oxygen breathing were significantly elevated in the group exposed to 0.51 mg/m³ PbClBr. These latter differences were not seen in the group exposed to the combination of 66.43 ppm CO plus 0.47 mg/m³ PbClBr.

Statistical analyses comparing the control group to the group exposed to 65.46 ppm CO indicated a significant mean difference in the number of breaths to 1% nitrogen, respiratory rate, and tidal volume measured during pure oxygen breathing. However, these differences were attributed to alteration of the sex ratio and hence the animal size distribution due to the deaths (not compound-related) of two male members of the group exposed to 65.46 ppm CO.

Microscopic alterations related to the exposure to PbClBr were found in the kidneys of the animals of these two lead groups. These histopathological changes were characterized by varying degrees of degeneration of the proximal convoluted tubules. The epithelial cells of these tubules were vacuolated and possessed vesiculated nuclei. Numerous intranuclear acid fast inclusion bodies were seen in these epithelial cells.



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Hematological, clinical biochemical, and arterial blood gas measurements made pre-exposure and periodically throughout the exposure period on the animals in the control and exposed groups did not reveal any meaningful differences. No trends were noted in any of these variables, and, in general, the exposed animals were comparable to the controls. Statistical analysis of the body weights measured periodically throughout the exposure period revealed that all animals in both the control and exposed groups increased in weight with time, although the group exposed to 65.46 ppm CO showed a slower mean growth rate which can be attributed to the deaths of two of its male members. No meaningful differences from the controls in terminal body weights, organ weights, and organ/body weight ratios were found for the exposed animals.



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Appendix D - Data compilations and summary of statistical analysis for

Statistical Grouping D, comprised of the following:

Group I - Control, Group II - 65.46 ppm CO, Group III -

0.51 mg/m³ PbClBr, and Group IV - 66.43 ppm CO + 0.47 mg/m³ PbClBr.

Table 1 - Monthly means and the grand mean for the analytical concentrations of carbon monoxide in Group II.

Date	n	$\bar{x}$ ppm	S.D.
4/ 7/68 - 4/31/68	24	52.7229	18.6179
5/ 1/68 - 5/31/68	31	64.9476	3.5378
6/ 1/68 - 6/30/68	30	66.0280	3.2531
7/ 1/68 - 7/31/68	31	65.6890	3.3289
8/ 1/68 - 8/31/68	31	65.2639	2.3260
9/ 1/68 - 9/30/68	30	63.8380	5.0975
10/ 1/68 - 10/31/68	31	63.9106	3.2811
11/ 1/68 - 11/30/68	30	65.2470	2.8750
12/ 1/68 - 12/31/68	31	66.2948	4.1978
1/ 1/69 - 1/31/69	31	65.3729	1.8454
2/ 1/69 - 2/28/69	28	66.9978	2.1481
3/ 1/69 - 3/31/69	31	65.9987	2.4073
4/ 1/69 - 4/30/69	20	67.5077	2.3761
5/ 1/69 - 5/31/69	31	68.1716	2.2823
6/ 1/69 - 6/30/69	30	68.4580	1.9130
7/ 1/69 - 7/31/69	31	66.8609	1.2850
8/ 1/69 - 8/31/69	31	67.4058	1.3534
9/ 1/69 - 9/30/69	30	65.5323	1.9411
10/ 1/69 - 10/31/69	31	65.6203	1.4197
11/ 1/69 - 11/30/69	30	67.1127	1.8847
12/ 1/69 - 12/31/69	31	64.7923	3.4599
1/ 1/70 - 1/31/70	31	65.1948	2.1385
2/ 1/70 - 2/28/70	28	66.7646	2.7352
3/ 1/70 - 3/31/70	31	65.8845	1.7923
4/ 1/70 - 4/ 9/70	9	64.8081	5.7551

N = 25

$\bar{x}$ = 65.46

S.D. = 3.33

Table 2 - Monthly means and the grand mean for the analytical concentrations of lead chlorobromide in Group III.

Date	n	$\bar{x}$ mg/m ³	S.D.
5/11/68 - 5/31/68	20	0.8570	1.0552
6/ 1/68 - 6/30/68	30	0.4743	0.6379
7/ 1/68 - 7/31/68	31	0.4565	0.3048
8/ 1/68 - 8/31/68	31	0.6022	0.1088
9/ 1/68 - 9/30/68	30	0.5773	0.1526
10/ 1/68 - 10/31/68	31	0.5074	0.1497
11/ 1/68 - 11/30/68	30	0.4286	0.1944
12/ 1/68 - 12/31/68	31	0.4638	0.1819
1/ 1/69 - 1/31/69	31	0.4752	0.1339
2/ 1/69 - 2/28/69	28	0.6154	0.7173
3/ 1/69 - 3/31/69	31	0.5677	0.1515
4/ 1/69 - 4/30/69	30	0.5147	0.2131
5/ 1/69 - 5/31/69	31	0.7770	0.1710
6/ 1/69 - 6/30/69	30	0.5503	0.1740
7/ 1/69 - 7/31/69	31	0.5597	0.2216
8/ 1/69 - 8/31/69	31	0.5010	0.1545
9/ 1/69 - 9/30/69	30	0.4737	0.2049
10/ 1/69 - 10/31/69	31	0.5352	0.2722
11/ 1/69 - 11/30/69	30	0.4930	0.0363
12/ 1/69 - 12/31/69	31	0.3871	0.1065
1/ 1/70 - 1/31/70	31	0.4052	0.2503
2/ 1/70 - 2/28/70	28	0.5100	0.3669
3/ 1/70 - 3/31/70	31	0.5561	0.2526
4/ 1/70 - 4/30/70	30	0.3079	0.5732
5/ 1/70 - 5/ 5/70	5	0.1180	0.0295

N = 25

$\bar{x}$ = 0.51

S.D. = 0.27

Table 3 - Monthly means and the grand mean for the analytical concentrations of carbon monoxide and lead chloride for Group IV.

Date	n	CO		PbClBr	
		$\bar{x}$ ppm	S.D.	$\bar{x}$ mg/m ³	S.D.
6/ 1/68 - 6/30/68	30	66.0710	2.5214	0.5133	0.2977
7/ 1/68 - 7/31/68	31	66.4219	2.2956	0.4619	0.2142
8/ 1/68 - 8/31/68	31	65.9890	3.0532	0.5868	0.1252
9/ 1/68 - 9/30/68	30	66.5103	3.7002	0.6360	0.2128
10/ 1/68 - 10/31/68	31	64.8868	3.8590	0.4477	0.1979
11/ 1/68 - 11/30/68	30	64.2883	3.2099	0.3627	0.1645
12/ 1/68 - 12/31/68	31	65.0668	2.3887	0.5590	0.2247
1/ 1/69 - 1/31/69	31	66.0261	1.8732	0.3787	0.1947
2/ 1/69 - 2/28/69	28	65.7504	1.7250	0.3350	0.2189
3/ 1/69 - 3/31/69	31	67.8374	2.1281	0.4634	0.1798
4/ 1/69 - 4/30/69	30	67.2590	2.0255	0.6210	0.3262
5/ 1/69 - 5/31/69	31	66.5474	2.1141	0.4374	0.1435
6/ 1/69 - 6/30/69	30	66.3283	1.3444	0.4703	0.1416
7/ 1/69 - 7/31/69	31	66.2529	1.4520	0.5313	0.1443
8/ 1/69 - 8/31/69	31	67.2252	2.1208	0.5042	0.1467
9/ 1/69 - 9/30/69	30	67.5253	2.2677	0.5493	0.1569
10/ 1/69 - 10/31/69	31	66.4932	2.0110	0.5365	0.2504
11/ 1/69 - 11/30/69	30	66.8467	1.4641	0.5010	0.2181
12/ 1/69 - 12/31/69	31	65.9313	2.8099	0.5203	0.1853
1/ 1/70 - 1/31/70	31	67.0703	2.1003	0.5419	0.2456
2/ 1/70 - 2/28/70	23	67.7143	1.9892	0.5368	0.1744
3/ 1/70 - 3/31/70	31	66.5290	1.5245	0.5568	0.3247
4/ 1/70 - 4/30/70	30	66.1123	1.8950	0.3607	0.2049
5/ 1/70 - 5/13/70	13	67.6277	2.7596	0.4669	0.2614

N = 24
 $\bar{x}$ = 66.43
S.D. = 2.28

N = 24
 $\bar{x}$ = 0.47
S.D. = 0.21

Table 4 - Summary of statistical analyses of body weight data for Statistical Grouping D, comprised of the following: Group I - Control, Group II - 65.46 ppm CO, Group III - 0.51 mg/m³ PbCl₂, and Group IV - 66.43 ppm CO + 0.47 mg/m³ PbCl₂.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	5.058	1.686	1.77	-
Error Deviation	902	8.583 x 10 ⁻²	9.515 x 10 ⁻⁴	-	-

FIRST DEGREE POLYNOMIAL REGRESSION COEFFICIENTS					
GROUPS	REGRESSION COEFFICIENTS ± S.E.		SV.X	n	r
	A	B			
I	2.63 ± 0.052	1.64 x 10 ⁻² ± 8.93 x 10 ⁻⁴	0.14	33	0.96
II	2.90 ± 0.065	9.97 x 10 ⁻³ ± 1.08 x 10 ⁻³	0.17	31	0.89
III	2.61 ± 0.046	1.53 x 10 ⁻² ± 8.02 x 10 ⁻⁴	0.13	33	0.97
IV	2.71 ± 0.049	1.29 x 10 ⁻² ± 8.31 x 10 ⁻⁴	0.13	32	0.95

Table 5 - Summary of statistical analyses of total respiratory system flow resistance during inspiration data for Statistical Grouping D, comprised of the following: Group I - Control, Group II - 65.46 ppm CO, Group III - 0.51 mg/m³ PbClBr, and Group IV - 66.43 ppm CO + 0.47 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	2.843 x 10 ⁻³	9.476 x 10 ⁻⁴	6.71	Yes
Error Deviation	1115	1.573 x 10 ⁻¹	1.411 x 10 ⁻⁴	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.					SV, x	n	r
	A	B	C	D				
I	0.044 ± 0.0033	2.12 x 10 ⁻⁴ ± 3.81 x 10 ⁻⁴	-9.72 x 10 ⁻⁶ ± 9.30 x 10 ⁻⁶	8.10 x 10 ⁻⁸ ± 6.10 x 10 ⁻⁸		0.008	39	0.37
II	0.042 ± 0.0038	1.34 x 10 ⁻⁴ ± 4.46 x 10 ⁻⁴	-2.29 x 10 ⁻⁷ ± 1.06 x 10 ⁻⁵	-7.00 x 10 ⁻⁹ ± 6.80 x 10 ⁻⁸		0.009	37	0.25
III	0.053 ± 0.0026	-5.52 x 10 ⁻⁴ ± 3.01 x 10 ⁻⁴	5.42 x 10 ⁻⁶ ± 7.35 x 10 ⁻⁶	-2.00 x 10 ⁻⁹ ± 4.86 x 10 ⁻⁸		0.006	39	0.65
IV	0.057 ± 0.0036	-6.36 x 10 ⁻⁴ ± 4.22 x 10 ⁻⁴	1.28 x 10 ⁻⁵ ± 1.07 x 10 ⁻⁵	-7.60 x 10 ⁻⁸ ± 7.30 x 10 ⁻⁸		0.008	37	0.39

Table 6 - Summary of statistical analyses of total respiratory system flow resistance during expiration data for Statistical Grouping D, comprised of the following: Group I - Control, Group II - 65.46 ppm CO, Group III - 0.51 mg/m³ PbClBr, and Group IV - 66.43 ppm CO + 0.47 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	1.314 × 10 ⁻³	4.381 × 10 ⁻⁴	4.16	Yes
Error Deviation	1115	1.174 × 10 ⁻¹	1.052 × 10 ⁻⁴	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.				Sy.x	n	r
	A	B	C	D			
I	0.042 ± 0.0028	-2.07 × 10 ⁻⁴ ± 3.26 × 10 ⁻⁴	-1.34 × 10 ⁻⁶ ± 7.97 × 10 ⁻⁶	2.90 × 10 ⁻⁸ ± 5.20 × 10 ⁻⁸	0.007	39	0.55
II	0.037 ± 0.0032	-1.36 × 10 ⁻⁴ ± 3.70 × 10 ⁻⁴	4.12 × 10 ⁻⁶ ± 8.84 × 10 ⁻⁶	-3.00 × 10 ⁻⁸ ± 5.70 × 10 ⁻⁸	0.007	37	0.12
III	0.046 ± 0.0023	-6.02 × 10 ⁻⁴ ± 2.70 × 10 ⁻⁴	7.30 × 10 ⁻⁶ ± 6.61 × 10 ⁻⁶	-1.90 × 10 ⁻⁸ ± 4.30 × 10 ⁻⁸	0.005	39	0.67
IV	0.047 ± 0.0029	-5.50 × 10 ⁻⁴ ± 3.48 × 10 ⁻⁴	1.05 × 10 ⁻⁵ ± 8.86 × 10 ⁻⁶	-6.10 × 10 ⁻⁸ ± 6.00 × 10 ⁻⁸	0.007	37	0.43

Table 7 - Summary of statistical analyses of tidal volume data for Statistical Grouping D, comprised of the following: Group I - Control; Group II - 65.46 ppm CO, Group III - 0.51 mg/m³ PbClBr, and Group IV - 66.43 ppm CO + 0.47 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION

SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	4.677 x 10 ⁺²	1.559 x 10 ⁺²	1.34	-
Error Deviation	847	9.821 x 10 ⁺⁴	1.159 x 10 ⁺²	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.			Sv.x	n	r
	A	B	C			
I	28.72 ± 1.92	2.52 x 10 ⁻¹ ± 1.88 x 10 ⁻¹	-2.46 x 10 ⁻³ ± 4.42 x 10 ⁻³	1.16 x 10 ⁻⁵ ± 2.84 x 10 ⁻⁵	32	0.77
II	31.47 ± 1.70	1.56 x 10 ⁻¹ ± 1.95 x 10 ⁻¹	7.12 x 10 ⁻⁴ ± 4.41 x 10 ⁻³	-1.79 x 10 ⁻⁵ ± 2.70 x 10 ⁻⁵	27	0.75
III	31.10 ± 1.75	1.64 x 10 ⁻² ± 1.72 x 10 ⁻¹	5.87 x 10 ⁻⁴ ± 4.10 x 10 ⁻³	3.20 x 10 ⁻⁶ ± 2.64 x 10 ⁻⁵	31	0.79
IV	32.88 ± 2.23	1.55 x 10 ⁻¹ ± 2.17 x 10 ⁻¹	-1.33 x 10 ⁻³ ± 5.30 x 10 ⁻³	4.90 x 10 ⁻⁵ ± 3.51 x 10 ⁻⁵	29	0.53

Table 8 - Summary of statistical analyses of respiratory rate data for Statistical Grouping D, comprised of the following: Group I - Control, Group II - 65.46 ppm tO, Group III - 0.51 mg/m³ PbClBr, and Group IV - 66.43 ppm CO + 0.47 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	1.203 x 10 ⁺³	4.010 x 10 ⁺²	6.37	Yes
Error Deviation	847	5.328 x 10 ⁺⁴	6.291 x 10 ⁺¹	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.					SV.X	n	r
	A	B	C	D				
I	40.74 ± 1.26	3.16 x 10 ⁻¹ ± 1.23 x 10 ⁻¹	-9.30 x 10 ⁻³ ± 2.90 x 10 ⁻³	5.63 x 10 ⁻⁵ ± 1.86 x 10 ⁻⁵		2.29	32	0.84
II	39.08 ± 1.15	1.51 x 10 ⁻¹ ± 1.32 x 10 ⁻¹	-4.01 x 10 ⁻³ ± 2.98 x 10 ⁻³	2.47 x 10 ⁻⁵ ± 1.83 x 10 ⁻⁵		1.97	27	0.42
III	37.85 ± 1.83	2.67 x 10 ⁻¹ ± 1.80 x 10 ⁻¹	-4.08 x 10 ⁻³ ± 4.28 x 10 ⁻³	1.39 x 10 ⁻⁵ ± 2.76 x 10 ⁻⁵		3.34	31	0.51
IV	40.34 ± 1.25	2.71 x 10 ⁻² ± 1.22 x 10 ⁻¹	-9.48 x 10 ⁻⁴ ± 2.97 x 10 ⁻³	7.80 x 10 ⁻⁶ ± 1.97 x 10 ⁻⁵		2.17	29	0.14

Table 9 - Summary of statistical analyses of dynamic compliance of the lung data for Statistical Grouping D, comprised of the following: Group I - Control, Group II - 65.46 ppm CO, Group III - 0.51 mg/m³ PbClBr, and Group IV - 66.43 ppm CO + 0.47 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	1.455 x 10 ⁺¹	4.851	1.06	-
Error Deviation	847	3.860 x 10 ⁺³	4.557	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.					n	r
	A	B	C	D	Sy.X		
I	6.01 ± 0.46	1.83 x 10 ⁻² ± 4.55 x 10 ⁻²	-1.88 x 10 ⁻⁴ ± 1.07 x 10 ⁻³	1.30 x 10 ⁻⁶ ± 6.90 x 10 ⁻⁶	0.84	32	0.43
II	6.35 ± 0.53	1.12 x 10 ⁻² ± 6.10 x 10 ⁻²	6.72 x 10 ⁻⁵ ± 1.38 x 10 ⁻³	-1.60 x 10 ⁻⁶ ± 8.40 x 10 ⁻⁶	0.91	27	0.24
III	6.09 ± 0.57	6.22 x 10 ⁻² ± 5.65 x 10 ⁻²	-1.12 x 10 ⁻³ ± 1.34 x 10 ⁻³	6.80 x 10 ⁻⁶ ± 8.70 x 10 ⁻⁶	1.05	31	0.45
IV	5.87 ± 0.55	4.24 x 10 ⁻² ± 5.38 x 10 ⁻²	-3.48 x 10 ⁻⁴ ± 1.31 x 10 ⁻³	6.00 x 10 ⁻⁷ ± 8.70 x 10 ⁻⁶	0.96	29	0.49

Table 10 - Summary of statistical analyses of pulmonary flow resistance data for Statistical Grouping D, comprised of the following: Group I - Control, Group II - 65.46 ppm CO, Group III - 0.51 mg/m³ PbClBr, and Group IV - 66.43 ppm CO + 0.47 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	2.783×10^{-3}	9.278×10^{-4}	6.48	Yes
Error Deviation	847	1.212×10^{-1}	1.431×10^{-4}	-	-

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THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.				Sy.x	n	r
	A	B	C	D			
I	0.024 ± 0.0036	7.84×10^{-5} ± 3.53×10^{-4}	8.71×10^{-7} ± 8.32×10^{-6}	-7.80×10^{-8} ± 5.30×10^{-8}	0.006	32	0.28
II	0.024 ± 0.0020	3.06×10^{-4} ± 2.32×10^{-4}	-6.56×10^{-6} ± 5.24×10^{-6}	2.40×10^{-8} ± 3.20×10^{-8}	0.003	27	0.83
III	0.025 ± 0.0039	8.93×10^{-6} ± 3.82×10^{-4}	-7.73×10^{-7} ± 9.10×10^{-6}	-3.00×10^{-9} ± 5.90×10^{-8}	0.007	31	0.45
IV	0.032 ± 0.0034	-1.07×10^{-4} ± 3.31×10^{-4}	-1.53×10^{-6} ± 8.08×10^{-6}	1.20×10^{-8} ± 5.30×10^{-8}	0.006	29	0.64

Table 11 - Summary of statistical analyses of work of breathing during inspiration per ml tidal volume data for Statistical Grouping D, comprised of the following: Group I - Control; Group II - 65.46 ppm CO, Group III - 0.51 mg/m³ PbClBr, and Group IV - 66.43 ppm CO + 0.47 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	1.141 x 10 ⁺¹	3.802	2.52	-
Error Deviation	847	1.278 x 10 ⁺³	1.509	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.					n	r
	A	B	C	D	Sy.x		
I	3.94 ± 0.30	-2.00 x 10 ⁻² ± 2.97 x 10 ⁻²	5.07 x 10 ⁻⁴ ± 7.00 x 10 ⁻⁴	-2.90 x 10 ⁻⁶ ± 4.50 x 10 ⁻⁶	0.55	32	0.25
II	3.97 ± 0.35	1.64 x 10 ⁻² ± 4.00 x 10 ⁻²	-3.57 x 10 ⁻⁴ ± 9.05 x 10 ⁻⁴	1.60 x 10 ⁻⁶ ± 5.50 x 10 ⁻⁶	0.60	27	0.30
III	4.13 ± 0.36	-7.58 x 10 ⁻² ± 3.54 x 10 ⁻²	1.49 x 10 ⁻³ ± 8.43 x 10 ⁻⁴	-7.90 x 10 ⁻⁶ ± 5.40 x 10 ⁻⁶	0.66	31	0.46
IV	4.30 ± 0.31	-3.83 x 10 ⁻² ± 3.03 x 10 ⁻²	5.35 x 10 ⁻⁴ ± 7.40 x 10 ⁻⁴	-2.10 x 10 ⁻⁶ ± 4.90 x 10 ⁻⁶	0.54	29	0.45

Table 12 - Summary of statistical analyses of work of breathing during expiration per ml tidal volume data for Statistical Grouping D, comprised of the following: Group I - Control; Group II - 65.46 ppm CO, Group III - 0.51 mg/m³ PbClBr, and Group IV - 66.43 ppm CO + 0.47 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	5.916 x 10 ⁻¹	1.972 x 10 ⁻¹	0.63	-
Error Deviation	847	2.650 x 10 ⁺²	3.128 x 10 ⁻¹	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.					r
	A	B	C	D	Sy.X	
I	1.85 ± 0.16	-2.66 x 10 ⁻² ± 1.60 x 10 ⁻²	5.49 x 10 ⁻⁴ ± 3.76 x 10 ⁻⁴	-3.00 x 10 ⁻⁶ ± 2.40 x 10 ⁻⁶	0.30	0.36
II	1.64 ± 0.14	5.80 x 10 ⁻³ ± 1.67 x 10 ⁻²	-2.09 x 10 ⁻⁴ ± 3.77 x 10 ⁻⁴	1.80 x 10 ⁻⁶ ± 2.30 x 10 ⁻⁶	0.25	0.37
III	1.73 ± 0.16	-2.15 x 10 ⁻² ± 1.57 x 10 ⁻²	3.97 x 10 ⁻⁴ ± 3.74 x 10 ⁻⁴	-1.80 x 10 ⁻⁶ ± 2.40 x 10 ⁻⁶	0.29	0.39
IV	1.72 ± 0.14	-2.30 x 10 ⁻³ ± 1.36 x 10 ⁻²	-1.72 x 10 ⁻⁴ ± 3.32 x 10 ⁻⁴	2.10 x 10 ⁻⁶ ± 2.20 x 10 ⁻⁶	0.24	0.50

Table 13 - Summary of statistical analyses of diffusing capacity of the lung for carbon monoxide data for Statistical Grouping D, comprised of the following: Group I - Control, Group II - 65.46 ppm CO, Group III - 0.51 mg/m³ PbClBr, and Group IV - 66.43 ppm CO + 0.47 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	1.212 x 10 ⁻¹	4.040 x 10 ⁻²	1.67	-
Error Deviation	902	2.180 x 10 ⁻¹	2.417 x 10 ⁻²	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.				SV.x	n	r
	A	B	C	D			
I	0.62 ± 0.031	3.04 x 10 ⁻³ ± 2.91 x 10 ⁻³	-2.49 x 10 ⁻⁵ ± 7.00 x 10 ⁻⁵	1.50 x 10 ⁻⁷ ± 4.60 x 10 ⁻⁷	0.052	33	0.78
II	0.69 ± 0.042	-3.51 x 10 ⁻⁴ ± 4.12 x 10 ⁻³	3.24 x 10 ⁻⁵ ± 9.79 x 10 ⁻⁵	-1.40 x 10 ⁻⁷ ± 6.40 x 10 ⁻⁷	0.069	31	0.64
III	0.67 ± 0.052	-3.37 x 10 ⁻³ ± 4.83 x 10 ⁻³	1.26 x 10 ⁻⁴ ± 1.16 x 10 ⁻⁴	-7.50 x 10 ⁻⁷ ± 7.70 x 10 ⁻⁷	0.087	33	0.68
IV	6.97 ± 0.039	3.64 x 10 ⁻³ ± 3.64 x 10 ⁻³	1.07 x 10 ⁻⁵ ± 8.76 x 10 ⁻⁵	-4.80 x 10 ⁻⁷ ± 5.80 x 10 ⁻⁷	0.065	32	0.82

Table 14. Summary of statistical analyses of number of breaths to 1% nitrogen data for Statistical Grouping D, comprised of the following: Group I - Control, Group II - 65.46 ppm CO, Group III - 0.51 mg/m³ PbClBr, and Group IV - 66.43 ppm CO + 0.47 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	1.447 x 10 ⁻³	4.825 x 10 ⁻²	2.96	Yes
Error Deviation	879	1.432 x 10 ⁻⁵	1.630 x 10 ⁻²	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.					SY.X	n	r
	A	B	C	D				
I	42.85 ± 3.42	8.85 x 10 ⁻² ± 3.26 x 10 ⁻¹	1.08 x 10 ⁻³ ± 7.83 x 10 ⁻³	-2.10 x 10 ⁻⁵ ± 5.20 x 10 ⁻⁵		5.69	32	0.33
II	40.30 ± 2.08	4.97 x 10 ⁻¹ ± 2.05 x 10 ⁻¹	-1.36 x 10 ⁻² ± 4.87 x 10 ⁻³	9.60 x 10 ⁻⁵ ± 3.20 x 10 ⁻⁵		3.42	31	0.58
III	44.77 ± 3.08	2.51 x 10 ⁻¹ ± 2.93 x 10 ⁻¹	1.16 x 10 ⁻³ ± 7.06 x 10 ⁻³	-3.40 x 10 ⁻⁵ ± 4.70 x 10 ⁻⁵		5.16	32	0.64
IV	37.67 ± 2.98	1.28 x 10 ⁻¹ ± 2.81 x 10 ⁻¹	6.80 x 10 ⁻³ ± 6.81 x 10 ⁻³	-7.70 x 10 ⁻⁵ ± 4.50 x 10 ⁻⁵		5.00	31	0.76

Table 15 - Summary of statistical analyses of respiratory rate (during oxygen breathing) data for Statistical Grouping D, comprised of the following: Group I - Control; Group II - 65.46 ppm CO, Group III - 0.51 mg/m³ PbClBr, and Group IV - 66.43 ppm CO + 0.47 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p $\leq$.05
Non-Parallelism	3	$4.212 \times 10^{+2}$	$1.404 \times 10^{+2}$	2.01	-
Error Deviation	879	$6.134 \times 10^{+4}$	$6.978 \times 10^{+1}$	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS $\pm$ S.E.					Sv.x	n	r
	A	B	C	D				
I	34.46 ± 1.11	2.49×10^{-1} $\pm 1.06 \times 10^{-1}$	-9.27×10^{-3} $\pm 2.54 \times 10^{-3}$	6.52×10^{-5} $\pm 1.63 \times 10^{-5}$		1.84	32	0.86
II	34.46 ± 1.13	2.14×10^{-1} $\pm 1.11 \times 10^{-1}$	-8.26×10^{-3} $\pm 2.64 \times 10^{-3}$	6.23×10^{-5} $\pm 1.73 \times 10^{-5}$		1.86	31	0.78
III	33.38 ± 1.80	1.91×10^{-1} $\pm 1.71 \times 10^{-1}$	-2.86×10^{-3} $\pm 4.13 \times 10^{-3}$	7.40×10^{-6} $\pm 2.72 \times 10^{-5}$		3.02	32	0.52
IV	37.76 ± 1.90	-3.73×10^{-2} $\pm 1.79 \times 10^{-1}$	1.21×10^{-3} $\pm 4.34 \times 10^{-3}$	-1.29×10^{-5} $\pm 2.88 \times 10^{-5}$		3.18	31	0.40

Table 16 - Summary of statistical analyses of cumulative tidal volume to 1% nitrogen data for Statistical Grouping D, comprised of the following: Group I - Control, Group II - 65.46 ppm CO, Group III - 0.51 mg/m³ PbClBr, and Group IV - 66.43 ppm CO + 0.47 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ .05
Non-Parallelism	3	1.933	6.444 x 10 ⁻¹	3.88	Yes
Error Deviation	879	1.460 x 10 ⁺²	1.661 x 10 ⁻¹	-	-

THIRD-DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.				SV.x	n	r
	A	B	C	D			
I	1.35 ± 0.09	5.79 x 10 ⁻³ ± 8.95 x 10 ⁻³	-1.38 x 10 ⁻⁵ ± 2.15 x 10 ⁻⁴	0.00 ± 1.40 x 10 ⁻⁶	0.16	32	0.70
II	1.45 ± 0.11	7.98 x 10 ⁻³ ± 1.12 x 10 ⁻²	-2.45 x 10 ⁻⁴ ± 2.68 x 10 ⁻⁴	2.00 x 10 ⁻⁶ ± 1.70 x 10 ⁻⁶	0.19	31	0.40
III	1.52 ± 0.07	4.55 x 10 ⁻⁴ ± 7.05 x 10 ⁻³	2.09 x 10 ⁻⁴ ± 1.70 x 10 ⁻⁴	-1.80 x 10 ⁻⁶ ± 1.10 x 10 ⁻⁶	0.12	32	0.82
IV	1.33 ± 0.10	-7.30 x 10 ⁻³ ± 9.41 x 10 ⁻³	4.57 x 10 ⁻⁴ ± 2.28 x 10 ⁻⁴	-3.60 x 10 ⁻⁶ ± 1.50 x 10 ⁻⁶	0.17	31	0.78

Table 17 - Summary of statistical analyses of tidal volume (during oxygen breathing) data for Statistical Grouping D, comprised of the following: Group I - Control, Group II - 65.46 ppm CO, Group III - 0.51 mg/m³ PbClBr, and Group IV - 66.43 ppm CO + 0.47 mg/m³ PbClBr.

ANALYSIS OF VARIANCE OF LINEAR REGRESSION					
SOURCE OF VARIATION	df	SS	MS	F	p ≤ 05
Non-Parallelism	3	1.293 x 10 ⁺³	4.311 x 10 ⁺²	4.18	Yes
Error Deviation	879	9.068 x 10 ⁺⁴	1.032 x 10 ⁺²	-	-

THIRD DEGREE POLYNOMIAL REGRESSION COEFFICIENTS

GROUPS	REGRESSION COEFFICIENTS ± S.E.					SY.X	n	r
	A	B	C	D				
I	39.08 ± 2.58	2.20 x 10 ⁻¹ ± 2.47 x 10 ⁻¹	-5.34 x 10 ⁻³ ± 5.92 x 10 ⁻³	4.68 x 10 ⁻⁵ ± 3.91 x 10 ⁻⁵		4.30	32	0.70
II	45.04 ± 3.49	-2.17 x 10 ⁻¹ ± 3.45 x 10 ⁻¹	5.40 x 10 ⁻³ ± 8.19 x 10 ⁻³	-3.26 x 10 ⁻⁵ ± 5.35 x 10 ⁻⁵		5.75	31	0.20
III	43.09 ± 2.17	-1.77 x 10 ⁻¹ ± 2.07 x 10 ⁻¹	3.84 x 10 ⁻³ ± 4.97 x 10 ⁻³	-1.63 x 10 ⁻⁵ ± 3.28 x 10 ⁻⁵		3.64	32	0.53
IV	44.88 ± 2.40	-3.52 x 10 ⁻¹ ± 2.27 x 10 ⁻¹	6.53 x 10 ⁻³ ± 5.50 x 10 ⁻³	-3.03 x 10 ⁻⁵ ± 3.64 x 10 ⁻⁵		4.03	31	0.47

Table 18 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for hematocrit (Hct. - percent) for male and female monkeys in Statistical Grouping D.

Groups	Pre-exposure -8	Time-Weeks			
		4	16	68	104
I - Control	36.4 (0.8)	36.0 (1.0)	33.1 (1.0)	37.3 (1.0)	36.7 (0.8)
II - 65.46 ppm CO	35.4 (1.0)	37.7 (1.0)	39.3 (0.8)	38.9 (0.7)	37.0 (0.7)
III - 0.51 mg/m ³ PbClBr	32.3 (0.8)	35.8 (0.8)	34.3 (0.9)	35.4 (1.1)	36.2 (0.9)
IV - 66.43 ppm CO + 0.47 mg/m ³ PbClBr.	36.8 (0.7)	31.7 (1.2)	39.2 (0.9)	39.8 (1.3)	40.3 (1.0)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Pre-exposure -8	Time-Weeks			
		4	16	68	104
PbClBr	N.S.	SIG	N.S.	N.S.	N.S.
CO	SIG	N.S.	SIG	SIG	SIG
Interaction	SIG	SIG	N.S.	N.S.	SIG

Table 19 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for hemoglobin (Hgb. = grams percent) for male and female monkeys in Statistical Grouping D.

Groups	Time-Weeks			
	Pre-exposure -8	4	16	68
I - Control	10.5 (0.3)	11.0 (0.3)	11.2 (0.2)	10.7 (0.3)
II - 65.45 ppm CO	10.9 (0.4)	11.5 (0.3)	10.5 (0.3)	11.9 (0.3)
III - 0.51 mg/m ³ PbClBr	10.2 (0.2)	9.6 (0.2)	10.4 (0.2)	10.4 (0.3)
IV - 66.43 ppm CO + 0.47 mg/m ³ PbClBr	11.3 (0.7)	10.5 (0.3)	12.3 (0.4)	11.8 (0.4)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks			
	Pre-exposure -8	4	16	68
PbClBr	N.S.	SIG	N.S.	N.S.
CO	N.S.	N.S.	N.S.	SIG
Interaction	N.S.	N.S.	SIG	N.S.

Table 20 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for total erythrocyte count (RBC - 10⁶/cmm) for male and female monkeys in Statistical Grouping D.

Groups	Pre-exposure -8	Time-Weeks			
		4	16	68	104
I - Control	5.44 (0.09)	5.44 (0.18)	5.70 (0.22)	5.10 (0.13)	6.13 (0.14)
II - 65.46 ppm CO	5.21 (0.13)	5.04 (0.17)	5.47 (0.14)	5.62 (0.31)	5.38 (0.14)
III - 0.51 mg/m ³ PbClBr	5.13 (0.18)	4.89 (0.20)	5.39 (0.30)	5.64 (0.23)	5.80 (0.19)
IV - 66.43 ppm CO + 0.47 mg/m ³ PbClBr	4.84 (0.13)	5.07 (0.17)	5.64 (0.19)	5.68 (0.25)	5.87 (0.18)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Pre-exposure -8	Time-Weeks			
		4	16	68	104
PbClBr	SIG	N.S.	N.S.	N.S.	N.S.
CO	N.S.	N.S.	N.S.	N.S.	N.S.
Interaction	N.S.	N.S.	N.S.	N.S.	SIG

Table 21 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for total leukocyte count (WBC - per cmm) for male and female monkeys in Statistical Grouping D.

Groups	Pre-exposure -8	Time-Weeks			
		4	16	68	104
I - Control	7240 (840)	7170 (290)	8670 (710)	8220 (680)	11940 (1110)
II - 65.46 ppm CO	11710 (1360)	10920 (850)	11260 (1040)	11380 (1720)	9480 (1130)
III - 0.51 mg/m ³ PbClBr	8430 (860)	11040 (3060)	9700 (930)	9110 (850)	8420 (870)
IV - 66.43 ppm CO + 0.47 mg/m ³ PbClBr	11040 (1320)	7100 (620)	12900 (1060)	10050 (1030)	8520 (550)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Pre-exposure -8	Time-Weeks			
		4	16	68	104
PbClBr	N.S.	N.S.	N.S.	N.S.	SIG
CO	SIG	N.S.	SIG	N.S.	N.S.
Interaction	N.S.	SIG	N.S.	N.S.	N.S.

Table 22 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for blood glucose (Glu. - mg percent) for male and female monkeys in Statistical Grouping D.

Groups	Time-Weeks			
	Pre-exposure -8	4	16	68
I - Control	59.3 (3.3)	59.5 (3.3)	69.0 (4.4)	97.3 (5.3)
II - 65.46 ppm CO	65.5 (4.4)	61.6 (2.6)	65.7 (3.0)	75.2 (4.6)
III - 0.51 mg/m ³ PbClBr	68.3 (2.9)	52.0 (3.0)	80.0 (2.2)	93.4 (3.5)
IV - 66.43 ppm CO + 0.47 mg/m ³ PbClBr	79.5 (9.0)	73.3 (4.3)	105.8 (7.9)	57.1 (3.5)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks			
	Pre-exposure -8	4	16	68
PbClBr	SIG	N.S.	SIG	SIG
CO	N.S.	SIG	SIG	SIG
Interaction	N.S.	SIG	SIG	N.S.

Table 23 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for blood urea nitrogen (BUN - mg percent) for male and female monkeys in Statistical Grouping D.

Groups	Pre-exposure -8	Time-Weeks			
		4	16	68	104
I - Control	16.3 (1.0)	19.2 (1.4)	17.0 (0.6)	22.6 (0.7)	23.2 (1.1)
II - 65.46 ppm CO	16.6 (0.8)	16.0 (1.4)	15.4 (1.6)	22.4 (2.1)	26.2 (1.5)
III - 0.51 mg/m ³ PbClBr	14.4 (0.6)	15.8 (0.5)	8.8 (0.9)	22.6 (1.6)	19.8 (1.1)
IV - 66.43 ppm CO + 0.47 mg/m ³ PbClBr	18.5 (2.3)	13.4 (0.8)	18.0 (1.1)	27.2 (2.6)	14.6 (0.9)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Pre-exposure -8	Time-Weeks			
		4	16	68	104
PbClBr	N.S.	SIG	SIG	N.S.	SIG
CO	N.S.	SIG	SIG	N.S.	N.S.
Interaction	N.S.	N.S.	SIG	N.S.	SIG

Table 24 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for total serum bilirubin (mg percent) for male and female monkeys in Statistical Grouping D.

Groups	Time-Weeks				
	Pre-exposure -8	4	16	68	104
I - Control	0.27 (0.03)	0.26 (0.02)	0.26 (0.02)	0.29 (0.03)	0.50 (0.06)
II - 65.46 ppm CO	0.25 (0.03)	0.29 (0.06)	0.50 (0.03)	0.44 (0.08)	0.35 (0.03)
III - 0.51 mg/m ³ PbClBr	0.18 (0.01)	0.28 (0.02)	0.28 (0.02)	0.27 (0.01)	0.33 (0.01)
IV - 66.43 ppm CO + 0.47 mg/m ³ PbClBr	0.83 (0.33)	0.46 (0.05)	0.30 (0.02)	0.80 (0.09)	0.38 (0.02)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks				
	Pre-exposure -8	4	16	68	104
PbClBr	N.S.	N.S.	SIG	SIG	N.S.
CO	N.S.	SIG	SIG	SIG	N.S.
Interaction	N.S.	N.S.	SIG	SIG	SIG

Table 25 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for total serum protein (grams percent) for male and female monkeys in Statistical Grouping D.

Groups	Time-Weeks				
	Pre-exposure -8	4	16	68	104
I - Control	7.30 (0.13)	7.76 (0.13)	8.24 (0.10)	7.44 (0.13)	7.57 (0.09)
II - 65.46 ppm CO	7.88 (0.15)	7.35 (0.09)	7.76 (0.13)	7.42 (0.16)	7.91 (0.15)
III - 0.51 mg/m ³ PbClBr	7.53 (0.17)	7.74 (0.19)	7.75 (0.22)	7.00 (0.13)	7.29 (0.16)
IV - 66.43 ppm CO + 0.47 mg/m ³ PbClBr	7.91 (0.20)	7.68 (0.10)	7.77 (0.19)	7.75 (0.09)	6.84 (0.18)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks				
	Pre-exposure -8	4	16	68	104
PbClBr	N.S.	N.S.	N.S.	N.S.	SIG
CO	SIG	N.S.	N.S.	SIG	N.S.
Interaction	N.S.	N.S.	N.S.	SIG	SIG

Table 26 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for serum albumin (grams percent) for male and female monkeys in Statistical Grouping D.

Groups	Time-Weeks				
	Pre-exposure -8	4	16	68	104
I - Control	2.56 (0.14)	2.58 (0.05)	3.11 (0.06)	2.45 (0.11)	2.75 (0.06)
II - 65.46 ppm CO	2.47 (0.10)	2.56 (0.06)	2.56 (0.03)	2.82 (0.10)	2.80 (0.10)
III - 0.51 mg/m ³ PbClBr	2.41 (0.05)	2.80 (0.05)	2.49 (0.04)	2.56 (0.05)	2.59 (0.06)
IV - 66.43 ppm CO + 0.47 mg/m ³ PbClBr	2.60 (0.14)	2.80 (0.10)	2.53 (0.09)	2.76 (0.05)	2.47 (0.09)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks				
	Pre-exposure -8	4	16	68	104
PbClBr	N.S.	SIG	SIG	N.S.	SIG
CO	N.S.	N.S.	SIG	SIG	N.S.
Interaction	N.S.	N.S.	SIG	N.S.	N.S.

Table 27 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for serum sodium (Na - mEq/liter) for male and female monkeys in Statistical Grouping D.

Groups	Time-Weeks			
	Pre-exposure -8	4	16	68
I - Control	148.0 (0.5)	143.7 (0.3)	139.2 (0.6)	145.8 (0.8)
II - 55.46 ppm CO	145.0 (0.4)	143.9 (1.0)	137.0 (0.5)	142.7 (0.9)
III - 0.51 mg/m ³ PbClBr	147.1 (0.4)	145.0 (0.6)	141.8 (0.5)	148.0 (0.5)
IV - 66.43 ppm CO + 0.47 mg/m ³ PbClBr	139.8 (1.9)	140.8 (1.2)	141.4 (0.4)	148.6 (0.7)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks			
	Pre-exposure -8	4	16	68
PbClBr	SIG	N.S.	SIG	SIG
CO	SIG	SIG	SIG	SIG
Interaction	SIG	SIG	N.S.	SIG

Table 28 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for serum potassium (K-mEq/liter) for male and female monkeys in Statistical Grouping D.

Groups	Pre-exposure -8	Time-Weeks			
		4	16	68	104
I - Control	3.75 (0.24)	3.67 (0.20)	3.64 (0.21)	4.02 (0.10)	3.56 (0.10)
II - 65.46 ppm CO	4.57 (0.17)	5.59 (0.56)	5.00 (0.32)	4.36 (0.20)	4.01 (0.14)
III - 0.51 mg/m ³ PbClBr	3.62 (0.09)	3.77 (0.24)	3.86 (0.18)	3.86 (0.15)	3.81 (0.23)
IV - 66.43 ppm CO + 0.47 mg/m ³ PbClBr	4.86 (0.59)	4.44 (0.13)	4.23 (0.18)	4.36 (0.18)	4.08 (0.14)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Pre-exposure -8	Time-Weeks			
		4	16	68	104
PbClBr	N.S.	N.S.	N.S.	N.S.	N.S.
CO	SIG	SIG	SIG	SIG	SIG
Interaction	N.S.	N.S.	SIG	N.S.	N.S.

Table 29 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for serum chlorides (Cl - mEq/liter) for male and female monkeys in Statistical Grouping D.

Groups	Pre-exposure -8	Time-Weeks			
		4	16	68	104
I - Control	111.9 (1.1)	109.7 (0.6)	108.4 (1.0)	110.2 (0.8)	112.8 (1.3)
II - 65.46 ppm CO	111.7 (0.9)	108.3 (1.0)	111.8 (1.5)	110.5 (0.6)	110.5 (0.7)
III - 0.51 mg/m ³ PbClBr	112.9 (0.5)	103.2 (0.4)	109.9 (0.6)	111.5 (0.8)	112.3 (0.4)
IV - 66.12 ppm CO + 0.47 mg/m ³ PbClBr	106.5 (2.6)	102.8 (1.0)	110.4 (1.2)	109.4 (0.4)	107.8 (0.7)

Comparison of Experimental Treatment Effects ($p < .05$)

Source of Variation

	Pre-exposure -8	Time-Weeks			
		4	16	68	104
PbClBr	N.S.	SIG	N.S.	N.S.	N.S.
CO	SIG	N.S.	N.S.	N.S.	SIG
Interaction	N.S.	N.S.	N.S.	N.S.	N.S.

Table 30 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for serum carbon dioxide (CO_2 - mEq/liter) for male and female monkeys in Statistical Grouping b.

Groups	Time-Weeks				
	Pre-exposure -8	4	16	68	104
I - Control	24.8 (1.0)	24.3 (0.8)	28.9 (0.7)	26.4 (0.7)	25.8 (0.6)
II - 65.46 ppm CO	26.5 (0.7)	28.3 (0.8)	25.2 (0.5)	21.3 (0.7)	26.2 (0.4)
III - 0.51 mg/m ³ PbClBr	26.7 (0.6)	25.7 (0.9)	22.9 (1.7)	26.5 (0.5)	24.6 (1.4)
IV - 66.43 ppm CO + 0.47 mg/m ³ PbClBr	22.1 (0.9)	24.7 (0.6)	27.6 (1.3)	24.7 (0.4)	25.8 (0.6)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation

	Time-Weeks				
	Pre-exposure -8	4	16	68	104
PbClBr	N.S.	N.S.	N.S.	SIG	N.S.
CO	N.S.	N.S.	N.S.	SIG	N.S.
Interaction	SIG	SIG	SIG	SIG	N.S.

Table 31 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for serum calcium (Ca - mg percent) for male and female monkeys in Statistical Grouping D.

Groups	Time-Weeks				
	Pre-exposure -8	4	16	68	104
I - Control	9.47 (0.22)	9.36 (0.11)	10.16 (0.08)	9.54 (0.30)	9.88 (0.12)
II - 65.46 ppm CO	9.66 (0.19)	9.41 (0.15)	9.18 (0.10)	9.54 (0.12)	10.01 (0.17)
III - 0.51 mg/m ³ PbClBr	9.77 (0.13)	9.32 (0.11)	9.34 (0.22)	9.90 (0.12)	10.01 (0.16)
IV - 66.43 ppm CO + 0.47 mg/m ³ PbClBr	10.06 (0.16)	8.91 (0.21)	10.47 (0.17)	9.52 (0.09)	9.04 (0.13)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation

Source of Variation	Time-Weeks				
	Pre-exposure -8	4	16	68	104
PbClBr	N.S.	N.S.	N.S.	N.S.	SIG
CO	N.S.	N.S.	N.S.	N.S.	SIG
Interaction	N.S.	N.S.	SIG	N.S.	SIG

Table 32 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for serum glutamic oxaloacetic transaminase (SGOT - K units) for male and female monkeys in Statistical Grouping D.

Groups	Pre-exposure -8	Time-Weeks			104
		4	16	68	
I - Control	26.0 (4.8)	45.4 (3.1)	20.2 (0.8)	97.3 (21.3)	47.0 (6.2)
II - 65.46 ppm CO	32.3 (3.2)	27.3 (2.3)	26.7 (1.3)	27.9 (1.4)	32.2 (4.6)
III - 0.51 mg/m ³ PbClBr	30.2 (2.1)	31.6 (2.2)	57.0 (10.7)	53.3 (4.5)	44.6 (5.4)
IV - 66.43 ppm CO + 0.47 mg/m ³ PbClBr	100.8 (21.2)	43.2 (5.0)	42.7 (5.4)	123.7 (27.0)	50.8 (3.0)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Pre-exposure -8	Time-Weeks			104
		4	16	68	
PbClBr	SIG	N.S.	SIG	N.S.	N.S.
CO	SIG	N.S.	N.S.	N.S.	N.S.
Interaction	SIG	SIG	N.S.	SIG	SIG

Table 33 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for serum glutamic pyruvic transaminase (SGPT - RF units) for male and female monkeys in Statistical Grouping D.

Groups	Time-Weeks				
	Pre-exposure -8	4	16	68	104
I - Control	15.4 (2.8)	20.7 (3.0)	25.1 (2.7)	41.4 (2.8)	40.8 (3.6)
II - 65.46 ppm CO	22.5 (3.1)	36.6 (4.1)	32.7 (1.9)	22.1 (1.3)	40.8 (3.5)
III - 0.51 mg/m ³ PbClBr	26.3 (2.5)	27.8 (1.5)	20.2 (3.0)	47.4 (0.7)	42.6 (8.1)
IV - 66.43 ppm CO + 0.47 mg/m ³ PbClBr	81.0 (13.9)	24.5 (1.5)	28.2 (2.4)	33.7 (2.1)	31.9 (2.1)

Comparison of Experimental Treatment Effects (p < .05)

Source of Variation	Time-Weeks				
	Pre-exposure -8	4	16	68	104
PbClBr	SIG	N.S.	N.S.	SIG	N.S.
CO	SIG	SIG	SIG	SIG	N.S.
Interaction	SIG	SIG	N.S.	N.S.	N.S.

Table 34 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for lactic acid dehydrogenase (LDH - WROB units) for male and female monkeys in Statistical Grouping D.

Groups	Time-Weeks			
	Pre-exposure -8	4	16	104
I - Control	513 (99)	746 (48)	573 (80)	1574 (156) 597 (93)
II - 65.46 ppm CO	800 (149)	484 (80)	600 (115)	661 (85) 452 (52)
III - 0.51 mg/m ³ PbClBr	926 (56)	794 (82)	822 (173)	1306 (129) 440 (41)
IV - 0.43 ppm CO + 0.47 mg/m ³ PbClBr	635 (60)	983 (87)	695 (54)	1412 (200) 638 (63)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation

	Time-Weeks			
	Pre-exposure -8	4	16	104
PbClBr	N.S.	SIG	N.S.	N.S.
CO	N.S.	N.S.	N.S.	N.S.
Interaction	SIG	SIG	N.S.	SIG

Table 35 - Mean values $\pm$ (S.E.) and summary of factorial analysis of variance for alkaline phosphatase (Alk. P04 - KA units) for male and female monkeys in Statistical Grouping D.

Groups	Time-Weeks				
	Pre-exposure -8	4	16	68	104
I - Control	57.2 (17.3)	58.6 (8.8)	55.2 (8.3)	41.9 (7.3)	48.4 (8.6)
II - 65.46 ppm CO	53.0 (5.9)	38.1 (3.4)	52.4 (6.2)	45.4 (5.7)	42.5 (8.0)
III - 0.51 mg/m ³ PbClBr	54.4 (8.6)	50.7 (6.9)	67.5 (9.9)	49.2 (8.4)	41.4 (7.6)
IV - 65.43 ppm CO + 0.47 mg/m ³ PbClBr	58.0 (12.7)	40.3 (4.7)	93.3 (23.9)	46.6 (6.0)	36.4 (4.9)

Comparison of Experimental Treatment Effects ($p \leq .05$)

Source of Variation	Time-Weeks				
	Pre-exposure -8	4	16	68	104
PbClBr	N.S.	N.S.	N.S.	N.S.	N.S.
CO	N.S.	SIG	N.S.	N.S.	N.S.
Interaction	N.S.	N.S.	N.S.	N.S.	N.S.

Table 36 - Mean values $\pm$ (S.E.) for blood gas and pH variables measured in male and female monkeys in Statistical Grouping D, comprised of the following: Group I - Control, Group II - 65.46 ppm CO, Group III - 0.51 mg/m³ PbClBr, and Group IV - 66.43 ppm CO + 0.47 mg/m³ PbClBr.

Interval Week	PO ₂				PCO ₂				pH			
	Group I	Group II	Group III	Group IV	Group I	Group II	Group III	Group IV	Group I	Group II	Group III	Group IV
-3	91.6 (2.0)	92.4 (1.0)	87.4 (1.7)	86.9 (1.5)	39.9 (0.7)	39.6 (1.2)	41.0 (0.8)	41.8 (0.9)	7.38 (0.00)	7.38 (0.01)	-	7.35 (0.01)
1	87.8 (1.8)	89.2 (1.6)	91.9 (2.7)	84.2 (1.5)	37.2 (1.0)	38.8 (1.3)	43.8 (1.2)	46.1 (1.7)	7.37 (0.00)	7.39 (0.01)	7.35 (0.01)	7.37 (0.00)
6	87.8 (1.9)	92.4 (0.9)	88.9 (1.9)	93.1 (1.9)	44.4 (1.0)	43.8 (1.4)	37.9 (1.1)	41.6 (0.9)	-	7.34 (0.01)	7.37 (0.00)	7.35 (0.01)
13	87.5 (0.9)	90.8 (1.8)	90.5 (1.3)	86.3 (1.2)	39.6 (1.3)	37.1 (0.9)	38.2 (1.1)	39.9 (1.1)	7.37 (0.00)	7.37 (0.00)	7.37 (0.01)	7.38 (0.01)
26	89.6 (1.9)	92.4 (1.7)	84.5 (1.1)	86.3 (1.3)	40.3 (1.2)	39.4 (1.0)	38.7 (0.6)	38.2 (1.1)	7.38 (0.01)	7.38 (0.00)	7.37 (0.01)	7.38 (0.00)
39	85.8 (1.2)	86.7 (1.2)	88.4 (1.1)	87.6 (1.0)	40.4 (1.8)	36.3 (1.1)	37.4 (1.3)	45.7 (1.0)	7.38 (0.00)	7.35 (0.01)	7.35 (0.01)	7.36 (0.00)
65	86.5 (1.6)	85.6 (1.4)	86.5 (1.7)	-	46.1 (1.6)	38.8 (1.3)	47.4 (0.8)	-	7.38 (0.00)	7.38 (0.00)	7.36 (0.00)	-
78	91.6 (1.6)	93.7 (1.4)	97.7 (2.4)	94.8 (1.9)	42.2 (1.4)	44.8 (0.9)	51.9 (1.1)	46.4 (1.2)	7.35 (0.01)	7.37 (0.01)	7.34 (0.01)	7.36 (0.00)
91	98.5 (2.6)	88.1 (1.1)	94.5 (2.4)	88.6 (1.3)	51.1 (2.4)	49.4 (1.3)	49.8 (1.5)	44.1 (0.9)	7.37 (0.01)	7.38 (0.01)	7.39 (0.01)	7.36 (0.00)
104	96.4 (2.2)	94.9 (2.0)	83.7 (1.0)	82.7 (1.0)	39.8 (1.5)	40.1 (1.6)	39.1 (0.9)	43.7 (1.4)	7.36 (0.01)	7.35 (0.00)	7.34 (0.00)	7.38 (0.00)

Table 37 - Mean values $\pm$ (S.D.) and summary of single classification analysis of variance for terminal body weight (g.), organ weight (g.), and organ/body weight ratios (%) for male monkeys for Statistical Grouping D, comprised of the following:
Group I - Control, Group II - 66.46 ppm CO, Group III - 0.57 mg/m³ PbCl₂Br, and Group IV - 66.43 ppm CO + 0.47 mg/m³ PbCl₂Br.

Groups	Terminal Body Weight	Brain	Thyroid	Lung	Heart	Liver	Kidneys	Adrenals
		wt. ratio	wt. ratio	wt. ratio	wt. ratio	wt. ratio	wt. ratio	wt.* ratio
I	4920 (1410)	73.8 (7.7)(0.31)	0.53 (0.34)(0.004)	27.8 (6.0)(0.08)	16.6 (4.6)(0.05)	88.1 (13.3)(0.25)	18.6 (4.6)(0.05)	0.63 (0.13)(0.002)
II	4067 (907)	67.9 (4.5)(0.26)	0.44 (0.14)(0.002)	23.7 (2.9)(0.08)	14.6 (2.3)(0.02)	74.1 (10.7)(0.17)	14.7 (1.8)(0.03)	0.61 (0.24)(0.003)
III	4720 (2252)	67.3 (3.5)(0.45)	0.41 (0.13)(0.003)	28.2 (9.9)(0.07)	16.4 (7.4)(0.01)	84.8 (26.6)(0.27)	18.3 (7.6)(0.05)	0.76 (0.35)(0.003)
IV	4480 (1121)	60.2 (6.3)(0.35)	0.38 (0.15)(0.004)	23.7 (4.4)(0.09)	15.8 (4.3)(0.05)	82.3 (14.6)(0.28)	17.9 (4.1)(0.05)	0.58 (0.03)(0.005)
Significant Differences (p $\leq$.05)								
I vs II	N.S.	N.S. N.S.	N.S.	N.S.	N.S. N.S.	N.S. N.S.	N.S. N.S.	N.S. N.S.
I vs III	N.S.	N.S. N.S.	N.S.	N.S.	N.S. N.S.	N.S. N.S.	N.S. N.S.	N.S. N.S.
I vs IV	N.S.	SIG N.S.	N.S.	N.S.	N.S. N.S.	N.S. N.S.	N.S. N.S.	N.S. N.S.
II vs III	N.S.	N.S. N.S.	N.S.	N.S.	N.S. N.S.	N.S. N.S.	N.S. N.S.	N.S. N.S.
II vs IV	N.S.	N.S. N.S.	N.S.	N.S.	N.S. N.S.	N.S. N.S.	N.S. N.S.	N.S. N.S.
III vs IV	N.S.	N.S. N.S.	N.S.	N.S.	N.S. N.S.	N.S. N.S.	N.S. N.S.	N.S. N.S.

* The variance of this group was heterogeneous.

Table 38 - Mean values $\pm$ (S.D.) and summary of single classification analysis of variance for terminal body weight (g.), organ weight (g.), and organ/body weight ratios (%) for female monkeys for Statistical Grouping D, comprised of the following: Group I - Control, Group II - 65.46 ppm CO, Group III - 0.51 mg/m³ PbClBr, and Group IV - 66.43 ppm CO + 0.47 mg/m³ PbClBr.

Groups	Terminal Body Weight	Brain	Thyroid	Lung	Heart	Liver	Kidneys	Adrenals
		wt. ratio	wt. ratio	wt. ratio	wt. ratio	wt. ratio	wt. ratio	wt. ratio
I	3075 (206)	59.5 (3.1)(0.13)	0.43 (0.09)(0.004)	21.6 (2.4)(0.08)	9.7 (0.8)(0.01)	66.3 (4.4)(0.17)	13.2 (1.4)(0.04)	0.76 (0.29)(0.010)
II	3475 (340)	58.4 (5.3)(0.18)	0.53 (0.20)(0.005)	22.4 (4.3)(0.09)	12.2 (0.5)(0.02)	77.5 (9.7)(0.08)	14.1 (1.6)(0.02)	0.78 (0.15)(0.006)
III	2750 (342)	58.9 (6.3)(0.32)	0.30 (0.11)(0.004)	20.7 (2.8)(0.05)	10.2 (2.7)(0.05)	59.0 (9.7)(0.14)	13.7 (1.8)(0.05)	0.69 (0.13)(0.002)
IV	3175 (330)	58.4 (8.4)(0.22)	0.48 (0.21)(0.005)	22.8 (3.9)(0.08)	10.1 (1.9)(0.03)	70.4 (11.0)(0.13)	14.1 (1.5)(0.04)	0.72 (0.13)(0.005)
Significant Differences (p $\leq$.05)								
I vs II	N.S.	N.S.	N.S.	N.S.	SIG	N.S.	N.S.	N.S.
I vs III	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.
I vs IV	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.
II vs III	SIG	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.
II vs IV	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.
III vs IV	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.

* The variance of this group was heterogeneous.

Table 39 - Histopathology incidence table for Statistical Grouping D,
comprised of the following: Group I - Control, Group II - 65.46 ppm
CO, Group III - 0.51 mg/m³ PbClBr, and Group IV - 66.43 ppm CO +
0.47 mg/m³ PbClBr.

	GROUPS			
	I	II	III	IV
LUNG				
Focal Pleural Thickening	2/9	4/9	2/9	2/9
Peribronchial Brown Pigment	1/9	1/9	3/9	2/9
Artifactual Emphysema	4/9	1/9	0/9	1/9
Alveolar Duct Fibrosis	9/9	0/9	2/9	4/9
Thickening Bronchiolar Wall	0/9	0/9	1/9	0/9
Bronchiolar Epithelial Hyperplasia	0/9	1/9	1/9	0/9
Bronchiolar Epithelial Hypertrophy	0/9	0/9	2/9	0/9
Pneumonocyte Hyperplasia	1/9	0/9	2/9	0/9
Peribronchial Lymphoid Hyperplasia	1/9	0/9	0/9	1/9
Emphysema	0/9	0/9	0/9	0/9
Focal Necrosis	0/9	1/9	0/9	0/9
Focal Hemorrhage	0/9	1/9	0/9	0/9
Parasite	0/9	0/9	0/9	0/9
Perivascular Edema	0/9	0/9	0/9	0/9
Pulmonary Edema	0/9	1/9	0/9	0/9
Bronchiolitis	1/9	0/9	0/9	0/9
Bronchitis	0/9	0/9	1/9	0/9
Monkey Pox	0/9	1/9	0/9	0/9
Vasculitis	1/9	0/9	0/9	0/9
Granuloma	0/9	0/9	0/9	0/9
Pneumonitis	0/9	1/9	0/9	0/9
Abscess	0/9	0/9	0/9	0/9
Lung Mite Infestation	1/9	0/9	0/9	0/9
Adenomatosis	0/9	0/9	0/9	0/9
Bronchiectasis	0/9	0/9	0/9	0/9
Purulent Pneumonia	0/9	0/9	0/9	0/9
Epithelial Necrosis	0/9	0/9	0/9	0/9
Thickened Alveolar Wall	0/9	0/9	1/9	1/9
Pleuritis	0/9	0/9	0/9	0/9
Crystallin Material (yellow)	0/9	0/9	2/9	0/9
Mucous	0/9	0/9	0/9	0/9
Focal Fibrosis	0/9	0/9	0/9	1/9
Pleural Fibrosis	0/9	0/9	0/9	1/9
Alveolar Wall Fibrosis	0/9	0/9	2/9	3/9
Vacuolated Media	0/9	0/9	0/9	0/9
Endothelial Hyperplasia	0/9	0/9	0/9	0/9
Stenotic	0/9	0/9	0/9	0/9
Chronic Pneumonia	0/9	0/9	0/9	0/9
Eroded Bronchi	0/9	0/9	0/9	0/9
Emphysematous Bulla	0/9	0/9	0/9	0/9

Table 39 - Continued

	GROUPS			
	<u>I</u>	<u>II</u>	<u>III</u>	<u>IV</u>
LUNG - Continued				
Atelectasis	0/9	0/9	0/9	0/9
Congested	0/9	0/9	0/9	0/9
Extravasated Blood	0/9	0/9	0/9	0/9
Collapsed Alveolar Wall	0/9	0/9	0/9	0/9
LIVER				
Pericholangitis	0/9	3/9	3/9	1/9
Bile Duct Proliferation	1/9	2/9	3/9	1/9
Focal Necrosis	0/9	1/9	0/9	1/9
Sinusoidal Pigment	2/9	2/9	2/9	0/9
Focal Hepatitis	0/9	0/9	0/9	0/9
Focal Lymphoid Infiltration	1/9	1/9	1/9	1/9
Nematodiasis	0/9	0/9	0/9	0/9
Thick Capsule	0/9	0/9	0/9	0/9
Granuloma	0/9	0/9	0/9	0/9
Abscess	0/9	0/9	0/9	0/9
Hepatocyte Vacuolation	0/9	2/9	1/9	3/9
Greenish Granular Material in the Hepatocytes	0/9	0/9	1/9	0/9
PERIBRONCHIAL LYMPH NODE				
Phagocytized Pigment	6/9	7/9	6/9	8/9
Lymphoid Activity	8/9	1/9	0/9	0/9
Lymphoid Atrophy	0/9	0/9	0/9	0/9
Adenitis	0/9	0/9	0/9	0/9
Granuloma	1/9	0/9	0/9	0/9
Reticuloendothelial Cell Hyperplasia	1/9	0/9	0/9	0/9
Lymphadenitis	0/9	0/9	0/9	0/9
TRACHEA				
Tracheitis	1/9	1/9	0/9	0/9
Increase in Goblet Cells	0/9	0/9	0/9	0/9
Exudate in Lumen	0/9	0/9	0/9	0/9
Necrosis of the Epithelium	0/9	1/9	0/9	0/9
Inclusion Bodies	0/9	1/9	0/9	0/9
Epithelial Hyperplasia	0/9	1/9	0/9	0/9
Cilia Atrophy	0/9	0/9	0/9	0/9
Squamous Metaplasia	0/9	0/9	0/9	0/9
Focal Hemorrhage	0/9	0/9	0/9	0/9

Table 39 - Continued

	GROUPS			
	<u>I</u>	<u>II</u>	<u>III</u>	<u>IV</u>
KIDNEY				
Interstitial Nephritis	0/9	4/9	2/9	1/9
Epithelial Vacuolation	1/9	1/9	3/9	4/9
Tubular Dilatation	3/9	0/9	0/9	0/9
Loss of the Brush Border	0/9	0/9	3/9	2/9
Nuclear Vesiculation	0/9	0/9	0/9	3/9
Tubular Hypertrophy	0/9	1/9	0/9	1/9
Pyelitis	0/9	0/9	0/9	0/9
Focal Mineralization	0/9	0/9	1/9	0/9
Glomerular Degeneration	0/9	1/9	0/9	0/9
Inclusion Bodies	0/9	0/9	7/9	5/9
Vasculitis	0/9	0/9	0/9	0/9
Congestion	0/9	0/9	0/9	0/9
Focal Fibrosis	0/9	1/9	0/9	1/9
Perirenal Abscess	0/9	0/9	0/9	0/9
Protein Inhibition	0/9	0/9	1/9	4/9
Intima Thickening	0/9	0/9	0/9	0/9
Endothelial Hyperplasia	0/9	0/9	0/9	0/9
HEART				
Focal Myocarditis	3/9	1/9	0/9	0/9
Endocarditis	0/9	0/9	0/9	0/9
Epicarditis	0/9	0/9	0/9	0/9
Myocardial Degeneration	1/9	0/9	0/9	0/9
Vasculitis	0/9	0/9	0/9	0/9
Subendocardial Hemorrhage	0/9	0/9	0/9	0/9
Thickened Endocardium	0/9	0/9	0/9	0/9
Focal Hyperplasia in the Endothelium	0/9	0/9	0/9	0/9
Intima Thickening	0/9	0/9	0/9	0/9
Granular Pigment	0/9	0/9	0/9	0/9



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VII. RESULTS OF THE SPECIAL HEMATOLOGICAL, SERUM BIOCHEMICAL, AND URINARY TESTS IN CYNOMOLGUS MONKEYS EXPOSED TO LEAD CHLOROBROMIDE ALONE AND IN BINARY COMBINATION WITH NO₂, SO₂, and CO.

This section describes only the results of special tests performed in monkeys from the control group and those exposed to PbClBr alone and in binary combination with NO₂, SO₂, and CO. Group numbers used throughout this section are presented in Table 14.

Table 14 - Group numbers for control group and PbClBr exposed groups

Group Designation (No.)	Agent	Nominal Concentration	Mean Analytical Concentration
I (1)	Control	0	0
II (9)	PbClBr	0.60 mg/m ³	0.51 mg/m ³
III (10)	NO ₂	0.50 ppm	0.48 ppm
	PbClBr	0.60 mg/m ³	0.54 mg/m ³
IV (18)	SO ₂	10.00 ppm	9.93 ppm
	PbClBr	0.60 mg/m ³	0.50 mg/m ³
V (20)	CO	67.50 ppm	66.43 ppm
	PbClBr	0.60 mg/m ³	0.47 mg/m ³

1. Osmotic Fragility of Erythrocytes Results

Results of the erythrocyte osmotic fragility studies performed during the last 24 weeks of the exposure period are presented in Table 15. Single classification analysis of variance revealed that relative to controls, all groups of monkeys exposed to PbClBr-contaminated atmospheres showed significantly decreased mean erythrocyte osmotic fragility, i.e., lower mean concentrations of NaCl at both 50 and 80 percent levels of hemolysis. The mean of the group exposed to PbClBr alone did not differ statistically from those of groups exposed to PbClBr in combination with NO₂, SO₂, and CO.



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Table 15 - Salt concentration ($\% \pm$ S.E.) resulting in 50% to 80% hemolysis of red blood cells from monkeys exposed to PbCl_2 alone and in binary combination and summary of single classification analysis of variance.

Group	% Hemolysis	
	50*	80*
I Control	0.354 (0.007)	0.316 (0.007)
II 0.51 mg/m^3 PbCl_2	0.284 (0.022)	0.212 (0.021)
III 0.48 ppm NO_2 0.54 mg/m^3 PbCl_2	0.269 (0.034)	0.194 (0.030)
IV 9.93 ppm SO_2 0.50 mg/m^3 PbCl_2	0.293 (0.021)	0.210 (0.030)
V 66.43 ppm CO 0.47 mg/m^3 PbCl_2	0.220 (0.028)	0.153 (0.025)

Groups	Significant Differences ($p < .05$)	
I versus II	Sig.	Sig.
I versus III	Sig.	Sig.
I versus IV	Sig.	Sig.
I versus V	Sig.	Sig.
II versus III	N.S.	N.S.
II versus IV	N.S.	N.S.
II versus V	N.S.	N.S.

* The variances of these groups were heterogeneous.



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2. Blood Lead Results

A plot of the mean values and faired curves for blood lead determinations measured during the pre-exposure control period and the 104 weeks of exposure are presented in Figure 82 for Groups I through V. As shown in this figure, the mean blood lead levels in all PbClBr-exposed groups increased to a higher level than the control group in the first few weeks of exposure and remained elevated throughout the study. The control group remained at essentially the same level throughout the exposure period. More variation was observed in the exposure groups than in the control group. Inspection of the curves indicated that the combination groups were not appreciably different from the group exposed to PbClBr alone.

3. Delta-Aminolevulinic Acid Results

Plots of the mean values and faired curves for measurement of delta-aminolevulinic acid (δ -ALA) in the urine are presented in Figure 83 for Groups I through V. This figure shows that mean δ -ALA levels increased early in the exposure period in all PbClBr exposed groups, and fluctuated at a higher level than control levels throughout the remainder of the study. Group V's δ -ALA level appeared to rise somewhat more slowly than those of Groups II, III, and IV.

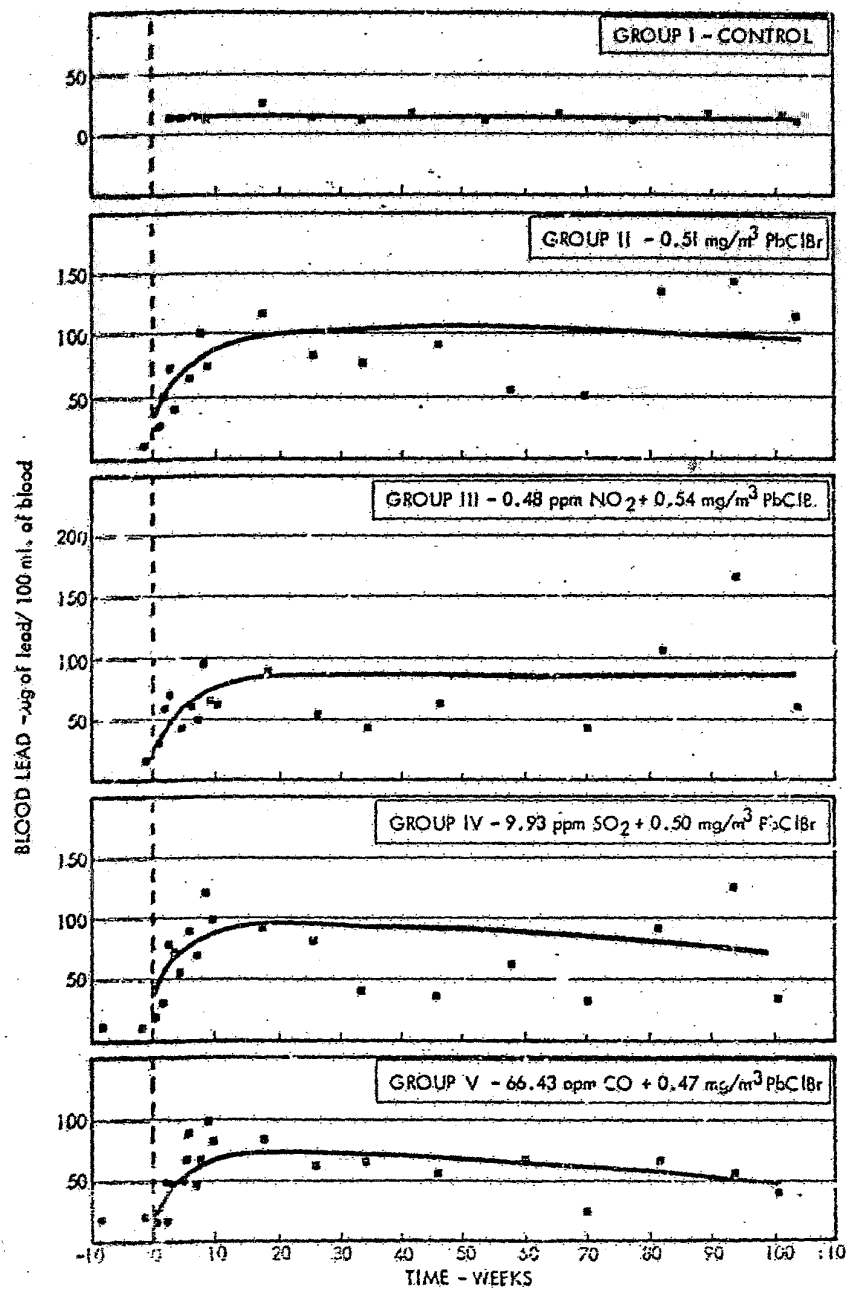


Figure 82 - Mean blood lead levels in monkeys exposed to PbCl₂ singly and in binary combination.

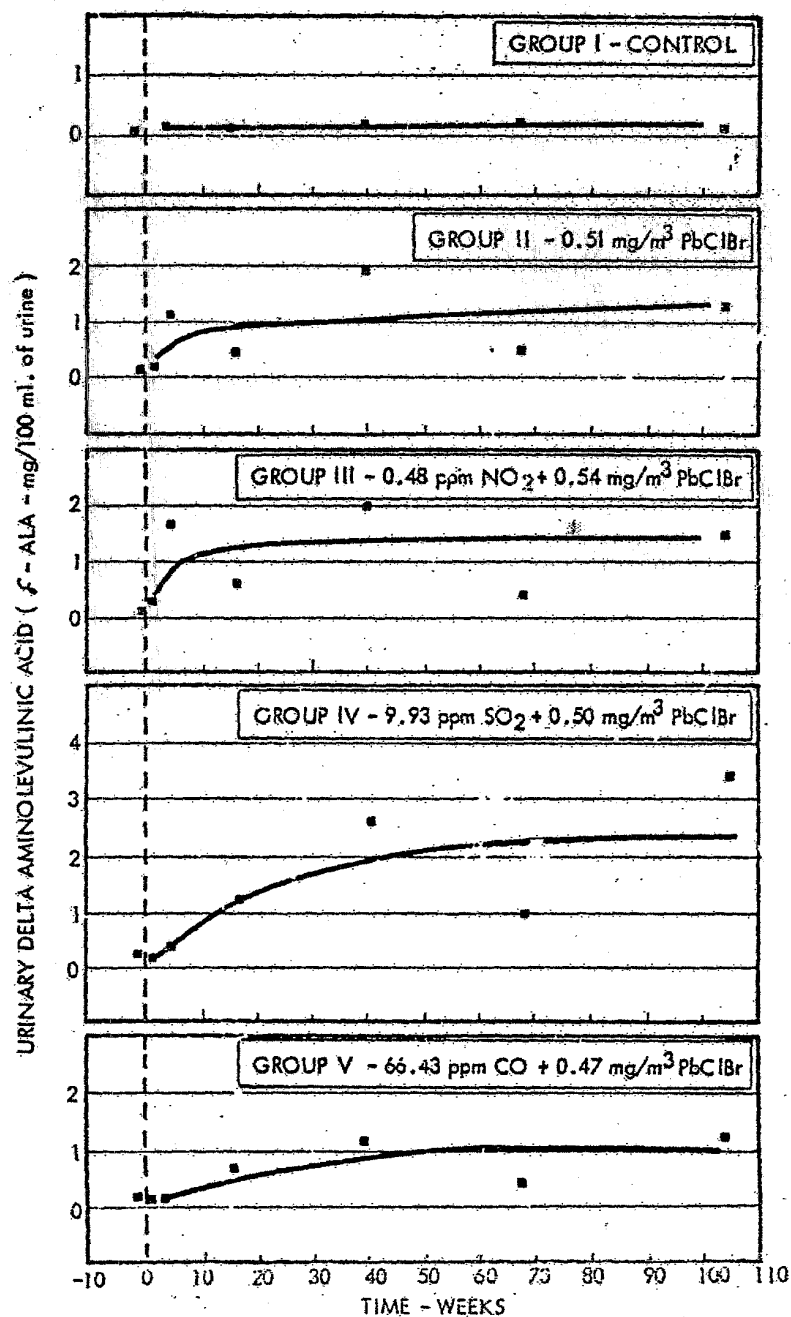


Figure 83 - Mean urinary δ -ALA levels in monkeys exposed to PbClBr singly and in binary combination.



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4. Urinary Coproporphyrin Results

Plots of the mean values and faired curves for urinary coproporphyrin determinations measured during the pre-exposure control period and the 104-week exposure period are presented in Figure 84. This figure indicates that the mean urinary coproporphyrin levels increased early in the exposure period in Groups II through V and remained at a higher level than Group I throughout the exposure period. Values for Group V (PbClBr + CO) appeared to increase more slowly than values for Groups II, III, and IV.

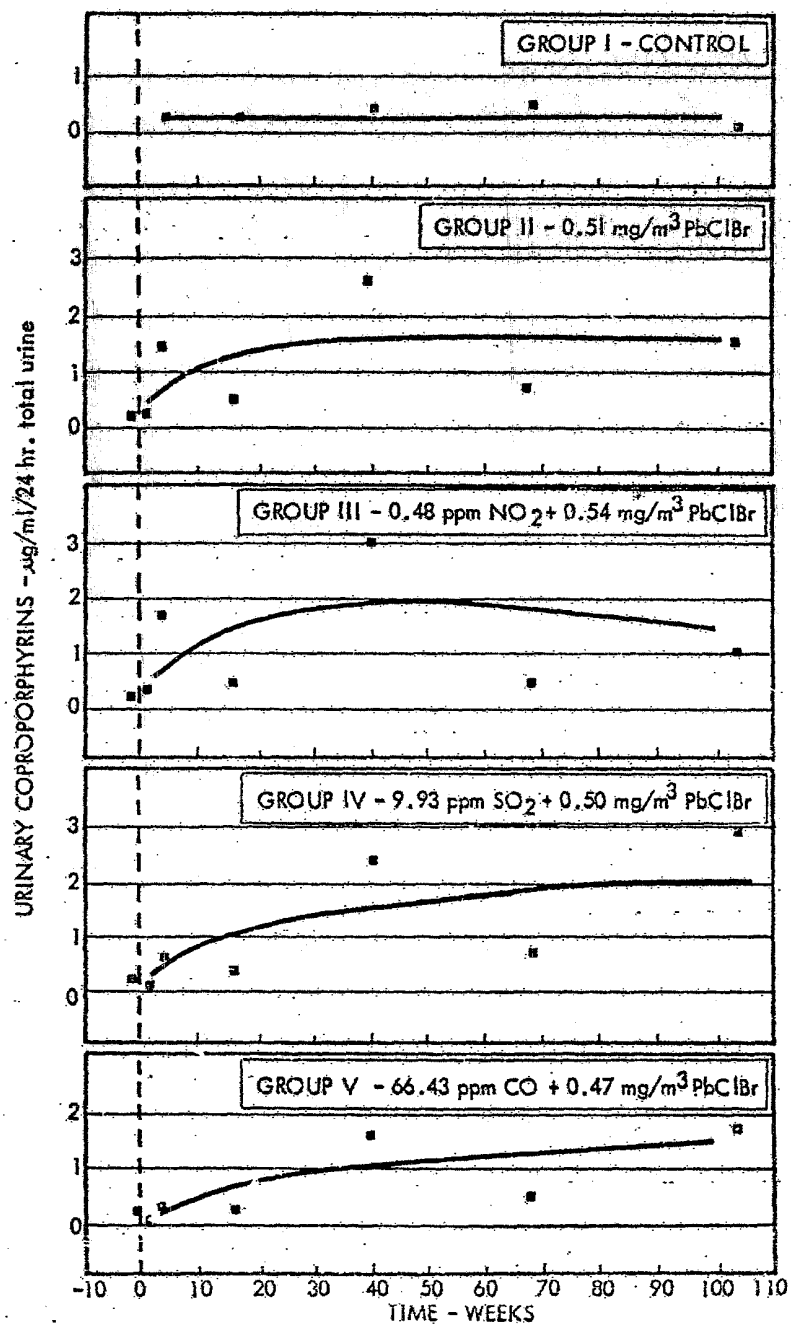


Figure 84 - Mean urinary coproporphyrin levels in monkeys exposed to PbClBr singly and in binary combination.



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VIII. Summary and Discussion of PbClBr Effects

The inhalation exposure of male and female cynomolgus monkeys to 0.51 mg/m^3 PbClBr for 104 weeks had an adverse effect on the distribution of ventilation which was not appreciably different from the effect of the binary combination of 0.54 mg/m^3 PbClBr and 0.48 ppm NO_2 , 0.50 mg/m^3 PbClBr and 9.93 ppm SO_2 , or 0.47 mg/m^3 PbClBr and 66.43 ppm CO . Thus there was no evidence of synergism among these combinations.

Similarly, exposure to these levels of PbClBr concentrations, alone or in the binary combinations, resulted in significant kidney effects characterized by degeneration of the proximal convoluted tubules.

All groups exposed to PbClBr showed decreased osmotic fragility of erythrocytes, increased blood lead, and delta-aminolevulinic acid levels, shortly after the beginning of exposure, and increased urinary coproporphyrin levels which tended to fluctuate in rhythm with the δ -ALA levels.



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