NERVE CONDUCTION VELOCITY - DOGS - rats

~~8 YEAR SACRIFICE~~

Manuscript "WORKING" SHEET

Ref. for ALAD as test of expos. to Lead

* Hernberg, S., J. Nikkanen, G. Mellin, and H. Lilius.
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Arch Environ. Health 21: 140-145, August 1970

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National Research Council. National Acad. Sci. Washington D.C. 1972
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* Hernberg S., and J. Nikkanen. "Enzyme Inhibition by Lead under
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Figure 1

Return ~~Recovery curves for~~ of blood lead concentration (upper grp), and of ALAD Activity (conc grp) of the Male Dogs in Group III. to Average ± 2 S.E. of Males in GROUP I.

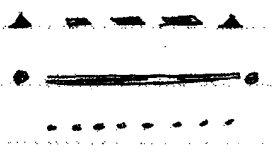

Figure 2.

Return of Urinary lead Concentration (upper grp) and Urinary Excretion of ALA (conc grp) of Male Dogs in Group III to Average

~~Re~~ Upper Grp: return of Urinary Lead Concentration towards the limit, ± 2 S.E, established

Figure 3

~~Regressions, with 95 %~~

Regressions ——— with 95 % confidence limits — · — · —, based on group averages, for return of blood lead concentrations ~~of dogs in groups II and III~~ to group I average. ~~for the dogs in Groups II and III.~~

Figure 4

Regression ——— and 95 % confidence limits — · — · —, based on group averages, for return of ALAD activity to group I average.

Figure 5

Slopes of ~~individual~~ blood lead concentration or recovery regressions ~~for each blood lead concentration~~ calculated for each dog in Group II versus the increase in its blood lead concentration resulting from the injection of lead.

Male □

Female ■

$r = -0.8371$ $r^2 = 0.7008$. (Significant at 1% level of probability).

Figure 6

Regression —— of the and its 95% confidence limits - - -

1 Logarithms of the slope of the ALAD recovery regression ~~calculated for~~ each Sa, day in groups II and III ~~versus~~ mean ~~the~~ his percent decrease in ALAD due to treatment with lead $r = 0.9474$ $r^2 = 0.8976$

r is sign at the 0.5% probability level.

Data of the "outlier" male in group II omitted for the calculation.

MR 701

THE EFFECT OF INORGANIC LEAD UPON THE CONDUCTION VELOCITY OF THE PERIPHERAL NERVES OF RATS AND DOGS

Medical Research Project No. MR-787

Among the insidious effects of inorganic lead upon animal tissue is its action upon peripheral neuromuscular structures. In lead poisoning clinical evidence of neuromuscular involvement may be absent; when present, it may vary from a mild weakness to paralysis of the musculature affected. "Wrist-drop or paralysis of other muscles may be fore-shadowed by gradual weakening or may occur without any premonitory symptoms and generally unpreceded by pain. The parts frequently affected are the extensors of the fingers, thumbs and wrists, but the muscles of the leg or feet are often attacked, sometimes the back, and in rare forms of poisoning the muscles of the eyes" (10). Today lead-exposed workers seldom develop muscular paralysis (1) due to preventive measures against lead absorption; however, any individual with clinical lead poisoning is a potential victim of this paralysis.

The site of this deleterious action of lead on the neuromuscular system has not been definitely established (5, 8, 9). There is some evidence that lead may affect the muscle directly by interfering with its metabolism (8). On the other hand, the demonstration of segmental demyelination of nerves obtained from lead-poisoned guinea pigs (5) is strong evidence that peripheral nerves are primary sites of the action of lead; the subsequent disturbance in the conduction of impulses along an injured nerve would account for the paralysis of the affected muscles. Finally, although evidence for this is lacking, lead might act at the motor end-plate, that microscopic area where the nerve fiber terminates in close proximity to the muscle fiber and where, probably by chemical means, the nerve impulse acts to initiate the muscular contraction. At this point,

interference with the excitation of the muscle fiber would also result in paralysis. Since most of the available clinical and pathological evidence favors the motor nerve as the prime target of the action of lead on peripheral neuromuscular structures (8), it was decided to try to detect the presence of peripheral nerve damage in animals fed lead acetate, using a physiological technique which could be utilized in the study of any potentially neurotoxic compound.

A physiological method for detecting peripheral nerve damage is the measurement of impulse conduction velocity between two points along a nerve trunk, a technique undergoing extensive clinical trial. Impulse conduction velocity is decreased in the area of a local compression lesion (12), in many cases of acute polyneuritis (2, 12), which finding may differentiate this condition from acute poliomyelitis (12), and in diabetes mellitus (3, 6, 13, 14, 16, 20). There have been several reports of slowed conduction along the ulnar nerve attributed to industrial poisons. These include 15 patients with occupational lead poisoning without neurological symptoms (18) and ten women with severe polyneuropathy associated with chronic triorthocresyl phosphate poisoning (17). In addition, "borderline" slowing was observed in two patients with lead neuropathy and in five with neuropathy due to the cutaneous absorption of an industrial solvent* (19). Animal experiments correlate slowed conduction velocity with clinical, and sometimes histological, evidence of nerve damage: in allergic polyneuritis in guinea pigs (11), in diphtheric polyneuritis in cats (15) and guinea pigs (11), in alloxan diabetes in rats (4) and, with histological confirmation, lead poisoning in guinea pigs (5).

In view of the clinical and experimental evidence correlating nerve damage with slowed conduction velocity, the use of velocity measurements for detecting peripheral nerve injury is promising. It was decided, therefore, to measure the

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* 85% trichloroethylene, 10% ethylene dichloride, 5% tritoluol phosphate.

conduction velocities of excised nerves, available at autopsy, from the rats and dogs in the two-year lead feeding study, MR-787, and in a small group of rats fed a higher level of lead.

METHODS

In principle, measurement of the impulse conduction velocity of an excised nerve fiber is straightforward, requiring only the measurement of the time it takes for the impulse to travel from one point of the fiber to another. If the distance between the two points is known, the velocity can be calculated. In practice, one end of the fiber is stimulated by passing an electric current through a short section, 3 to 5 mm, between two electrical contacts, the stimulating electrodes. The minute change in the membrane potential, known as the action potential, which is associated with the impulse as it travels along the fiber, is detected further along the nerve by another electrical contact, the recording electrode. This action potential is amplified and fed into a suitable recording device, usually a cathode ray oscilloscope.

In the present experiments, a nerve trunk containing many fibers was studied. Adequate "maximal" stimulation of a nerve trunk initiates impulses in all of the fibers; each impulse is conducted along its fiber at a rate characteristic of that fiber, rapidly in some, more slowly in others. The action potentials associated with the successive arrivals of the impulses at the recording electrode cause a sustained, sometimes complex, deflection of the oscilloscope beam called the "compound" action potential. At any selected point of the oscilloscope tracing, the magnitude of the deflection is a function of the number of impulses at the recording electrode at that particular instant.

I. Equipment

Figure 1 is a photograph of the equipment used in the experiments. From left to right in the photograph are 1) the constant temperature shelter in the right portion of which an electrode set is visible, 2) the telethermometer, 3) the stimulus isolation unit, 4) the recording unit consisting of amplifier and oscilloscope, and 5) the Tektronix stimulation unit.

A. Electrodes. Two electrode sets, one for dog nerves and a smaller one for rat, were designed by Paul E. Smith, Jr., and made by Edward F. Fabryka, of the Physics Section. Each set consists of a holder made from 1/4-inch Teflon® sheet supporting a horizontal row of equally spaced and parallel platinum wires (Figure 2). The first two wires at one end of the row serve as the stimulating electrodes, S_1, S_2; any two of the other wires may serve as recording electrodes*,R. (Two are necessary to complete the circuit through the recording device.)

B. Stimulator. In the earlier experiments a Grass square wave stimulator, Model S4G was used. It was replaced by a Tektronix unit assembled by Paul E. Smith, Jr.; it consists of a pair of Type 161 pulse generators each driven by a Type 162 wave-form generator. Both stimulators provide a stimulus which can be controlled as to duration, voltage, and frequency of application. The strength of the stimulus applied to a nerve was 4 to 10 volts and its duration was 0.06 to 0.1 mSec (milliseconds). In order to minimize the effect of the stimulus current

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* In addition to the stimulating electrodes, the small holder has nine recording electrodes spaced every 5 mm; maximum available conduction distance: 4 cm. The large holder has 20 recording electrodes spaced 10 mm apart, maximum conduction distance: 18.5 cm. In addition, the large set has "dummy" wires between electrodes to give added support to the nerve and minimize sagging.

upon the oscilloscope beam, an isolation unit, "3" in Figure 1, was placed in the stimulation circuit between the stimulator and the nerve: a Grass SIU 478 A isolation unit with the Grass stimulator and an Argonaut LIT 069 isolation transformer with the Tektronix.

C. Recording Equipment. Tektronix units were used. The nerve action potentials were amplified by a differential amplifier, Type 2A63 or Type 3A3 Dual Trace*, and fed into a Type 561A cathode ray oscilloscope. The sweep of the oscilloscope beam was triggered by a mechanism within the stimulator; the speed of the sweep was controlled by a Type 2B67 time base which has a range of 1 microsecond to 5 seconds per screen division. The oscilloscope tracing was photographed with a Tektronix C 12 camera unit using Polaroid Type 410 black and white land film. Measurements were made directly from the photographs.

D. Constant Temperature Shelter. During experiments nerves must remain moist and, in addition, mammalian nerves must be kept at or near body temperature, 37°C (98.6°F), if conduction velocities are to be equivalent to those in the intact animal. Mammalian nerves are usually mounted within a small protective chamber which is suspended in or above a water bath. In most of the present experiments, however, 16 to 20 nerves had to be tested daily so that a fresh nerve had to be mounted every 10 to 20 minutes and the temperature of even a small protective chamber could not be maintained by a water bath. Therefore a shelter,

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* Amplification range: Type 2A63: 20 volts to 1 millivolt per screen division.
Type 3A3: 10 volts to 0.1 millivolt per screen division.

provided with a continuous and adjustable supply of warm and moist air, was constructed.

The shelter* was 36 inches long by 18 inches wide; a sloping roof, 24 1/2 inches high in front and 12 1/2 inches in back, provided drainage for the water which condensed on its inner side. Within, the shelter was partitioned into a 19 1/2-inch by 18-inch "outer" chamber and a 16 1/2-inch by 18-inch "inner" chamber. The former had a permanent opening in front and was used for mounting the nerves on the electrodes while the latter sheltered the nerves while the action potentials were photographed. A thermistor probe suspended within 4 to 6 cm of the mounted nerve and connected to a deflection type meter, Tele-Thermometer Model 43, Type TF, permitted a direct reading of the dry bulb temperature of the inner chamber whenever desired.

An ample supply of warm, moist air for the shelter was provided by a constant-temperature room; with the temperature of this room at 43.06°C (109.5°F) dry bulb and 40.28°C (104.5°F) wet bulb, 87 percent relative humidity; the dry bulb temperature of the inner chamber was maintained at 37.06°C ± 0.4°C (98.7°F ± 0.72°F).

II. Nerve Preparations

The left hind leg of the animal was obtained from the Pathology Section and the nerve removed: tibialis from the dog and the sciatic with its

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* 1. Framework: Equipto Type 5700 hot dip galvanized slotted steel, 1 1/2" x 3" x 0.104".
2. Back wall which supported the warm air inlets: 1/4" Teflon® sheet.
3. Other walls, roof, and inner partition: 0.003" Mylar® sheeting.

tibialis branch from the rat. During dissection the nerve was protected against drying by the application of a lactated Ringer's solution* or by a silicone preparation**. The nerves were mounted so that the central end made contact with the stimulating electrodes, the peripheral end (tibialis branch of rat nerves) with the recording electrodes. The rat nerves required five to ten minutes, the larger dog nerves ten to 15 minutes, to adjust to the environment of the inner chamber as shown by the constancy of the velocity measurement.

III. The Oscilloscope Tracing and Its Measurement

A typical dual tracing***, copied from one obtained on a dog nerve, is shown in Figure 3. The sweep of the oscilloscope beam is from left to right; its speed 0.2 mSec per division of the screen. The lower response was recorded by an electrode 2.48 cm distal to the stimulating electrodes, the upper by an electrode 2 cm farther along the nerve. The following discussion applies to either response.

The first small upward deflection, A, lasting 0.1 mSec is due to the stimulus current and is called the stimulus or shock artifact. Since this current is conducted by the nerve as by a wire so that its arrival at the recording electrode is essentially instantaneous with its application to the nerve, it indicates the time of stimulation in the tracing. After a short delay,

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* Cutter's for injection.

** 360 medical fluid, viscosity grade 50 cstks. Supplied through the courtesy of the Medical Products Division, Dow-Corning Corporation.

*** Obtained with Type 3A3 amplifier which "splits" the beam so that the response to a single stimulus can be recorded from two points along the nerve during a single sweep of the oscilloscope beam.

0.25 mSec in the lower tracing and 0.44 mSec in the upper, there is a large diphasic deflection which is the compound action potential. The two measurements made by Eliasson (4) were adopted: the time from the start of the stimulus artifact 1) to the beginning of the upstroke of the action potential, the "inflection" 1, Figure 3, caused by the arrival of the most rapidly conducted impulses at the recording electrode, and 2) to the point of maximum deflection, the "peak" 2, Figure 3, due to the later arrival of the impulses over the largest number of similar fibers. These measurements provide the data for the calculation of "inflection" velocity and "peak" velocity, respectively.

IV. Animals Studied

A total of 262 rat and 33 dog nerves were tested. The dogs were electrocuted; the 224 rats of the 2-year feeding study were killed by being chloroformed. The other 38 rats comprised a special high lead dosage group killed by decapitation in order to determine whether chloroform had a significant effect on conduction velocity. Table I gives the groupings of the animals according to lead dosage level and duration of treatment.

RESULTS

I. Validity of Observed Conduction Velocities

A. Sciatic-Tibialis Nerves from Rats. The average conduction velocities with their standard deviations from the mean are given for each treatment group in Table I.

1. Nerves from decapitated rats. The nerves from the various groups of decapitated rats had inflection velocities which averaged from 67 to 73 m/sec (meters per second). These values

overlap those of 71 and 74 m/sec reported by Eliasson for nerves obtained from normal and starved decapitated rats (4). However, the averages for the peak velocity ranged from 41 to 45 m/sec, distinctly below his values of 53 and 55 m/sec.

2. Nerves from rats killed by chloroform. When comparisons are limited to the values for equal conduction distances, the nerves from the chloroformed rats of the 18-month treatment groups had higher, and those from the 24-month groups had lower conduction velocities than the nerves from the decapitated animals. Although the average values do not support the expectation that chloroform would depress conduction velocity, the larger standard deviations obtained for the measurements made on the nerves from the chloroformed rats indicate that these preparations are not as satisfactory as those obtained from the decapitated animals.

B. Tibialis Nerves from Dogs. Unfortunately, technical difficulties with stimulation prevented satisfactory recording of the action potentials of the nerves from the four male dogs of Group I, and three other dogs were killed before the scheduled autopsy date. However, the data obtained on all of the other nerves are given in Table II. Nerves from the male dogs had inflection velocities ranging from 83 to 105 m/sec and peak velocities ranging from 48 to 58 m/sec. The corresponding values for the nerves from the females were, respectively, 84 to 102 m/sec and 47 to 56 m/sec. These velocities are within the range for mammalian fibers as listed by Grundfest (7). Because the number of dogs per group is small and since the F test for difference in velocity due

to sex* was insignificant, the data from both sexes were used for calculation of the standard deviations for each treatment group. These standard deviations, ranging from ± 1.1 to ± 6.0 m/sec for inflection velocity and from ± 1.3 to ± 2.8 m/sec for peak velocity, are comparable to those obtained for the measurements made on nerves from the decapitated rats. This indicates that the preparations from electrocuted animals may be as satisfactory for conduction velocity studies as those from decapitated animals.

II. The Effect of Lead

Comparison of the conduction velocities of the nerves from the lead-fed animals with the values obtained for their respective controls does not reveal a decrease in velocity due to lead. This conclusion is substantiated by the results of the F test for effect of treatment** which was applied to all of the data obtained at each sacrifice, Table III. With the exception of a significant effect on the inflection velocity of the nerves from the dogs, $0.01 < P < 0.05$, lead had no effect on conduction velocity.

This effect of lead on inflection velocity is limited to the nerves obtained from the male dogs (Table III) and consists of a successive increase in velocity as the dosage increases from 10 to 100 ppm. At the dosage level of 500 ppm (Group V), the inflection velocity is reduced. This velocity increase is significant at the 5 percent level whether or not the data from Group V are included in the calculation of F. Other possible causes of this effect have been excluded: preparation time, order in which nerves were tested, and shelter

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* $F = \frac{\text{Variance due to Sex}}{\text{Variance within Group}}$

** $F = \frac{\text{Variance due to Treatment}}{\text{Variance within Group}}$

temperatures.

Examination of the velocity averages for the nerves from the rats of the 2-year feeding study which were sacrificed at 18 months shows the presence of a similar trend following an initial slowing; however, the trend in this case is statistically insignificant even when the data from the control groups (Groups I and Ia) are omitted from the calculation of F (Table III).

DISCUSSION

The values obtained for impulse conduction velocity in these experiments indicate that such measurements are both practical and valid when made on the type of preparation available at autopsy with the possible exception of those from the animals killed with chloroform.

I. Rats Killed with Chloroform

The nerve preparations from these animals might be considered unsatisfactory because of the difference in the average velocity values obtained for the nerves from the 18- and 24-month treatment groups and because of the within group variability. However, factors other than the chloroform may account for these discrepancies, such as the 6-month difference in age between two groups and/or an unexplained technical difficulty which results in an apparent decrease in conduction time when the shelter humidity is very high.

A. A decrease in conduction velocity with increasing age has been reported for the nerves from human subjects (3, 13, 14, 16); such a physiological decrease may account for the slower average velocities of the nerves from the older rats. The within group variability might be the result of differences in the amount of fiber deterioration

and/or in the amount of damage inflicted by the separation of the nerves from the dense layers of fat in which they were characteristically embedded, especially in the 24-month animals.

B. The technical difficulty is associated with high shelter humidity; it is prominent when the relative humidity is 90 per cent and higher. It results in an apparent decrease in conduction time* and calculation of an erroneously high conduction velocity. As the nerves from the 18-month rats were kept moist with Ringer's solution** during the dissection, a higher shelter humidity was required to prevent drying than was needed for the silicone-protected nerves from the 24-month animals. The higher velocities of the nerves from the younger rats may be due in part to this technical error.

II. The Effect of Lead

Since all of the nerves obtained during the same sacrifice were treated as nearly alike as possible, comparison of the velocities of the nerves from the treated animals with the values obtained for the controls killed during the same sacrifice is valid.

The absence of a significant lead effect on the rat nerves supports the observations of Dr. Fullerton who found that, in comparison with nerves from guinea pigs and rabbits, rat nerves are resistant to the toxic action of lead (5). No report on the action of lead on the peripheral nerves of dogs was located in the literature. At the time of autopsy, the male dogs had

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* Details under technical difficulties.

** Use of the silicone preparation began after the sacrifice of the 18-month rats.

significantly higher blood lead concentrations than the females ($p < 0.005$); this difference in blood lead concentrations correlates with the demonstration of a significant lead effect only for the nerves from the male dogs. At the time of sacrifice, all of the dogs appeared healthy and showed no clinical signs of peripheral neuropathy.

III. Technical Difficulties

For comparative purposes technical difficulties which cause variable results can be mostly eliminated or controlled.

A. The high humidity of the inner chamber causes a marked tendency for the action potential to move towards, and eventually fuse with, the stimulus artifact as the stimulator voltage is increased. This apparent shortening of the interval between stimulation and response results in the calculation of falsely high conduction velocities and the magnitude of the error (velocity increase) increases with the voltage used to stimulate the nerve. This error can be minimized by 1) using the silicone preparation so that a lower humidity suffices, 2) stimulating the nerves with the same stimulator voltage which must be supramaximal for all, 3) wiping the electrode holder before mounting each nerve, and 4) using a long conduction distance.

B. The effect of conduction distance per se observable in the data of the six-month group of the special study rats, Table I, can be eliminated if conduction distance is standardized.

C. Conduction time between two recording electrodes. Theoretically, because excitation time is excluded, measurement of the time it takes for impulses to travel the distance between two recording electrodes, rather than between stimulating and recording electrodes, should provide a more exact determination of conduction velocity. However, measurements of the intervals between the inflections, or between the peaks, of the action potentials obtained from two recording electrodes during a single sweep of the oscilloscope beam (Figure 3) provided velocity values which were so variable that this method of measurement has been abandoned temporarily.

D. Other causes of variability. Variables which, in these experiments, could not be correlated with conduction velocities included 1) the dry bulb temperature of the inner chamber which had a maximum variation of 1.1°C (1.98°F) and 2) surprisingly, the time which elapsed, 19 to 47 minutes*, between the death of the animal (chloroformed rats: from start of chloroform administration) and the placing of its nerve in the inner chamber. It is possible that the minimum delay between death and mounting, 19 minutes, is longer than some critical interval after which further delay has little additional effect.

CONCLUSIONS

1. Measurement of the impulse conduction velocities of excised nerves obtained from animals at the time of autopsy may provide physiological evidence of the presence of peripheral nerve damage due to the action of toxic compounds.

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* Special high lead dosage rats: this interval was shorter, ranging from 11 1/2 to 19 minutes.

2. Inorganic lead, as lead acetate, administered to rats in concentrations as high as 500 ppm daily for two years and in a concentration of 5000 ppm for 13 months had no significant effect on the impulse conduction velocity of the sciatic-tibialis nerves. In concentrations to 500 ppm for two years, lead had a significant effect ($0.01 < p < 0.05$) on the inflection velocity of the tibialis nerves of the male dogs. This effect consisted of a progressive increase in inflection velocity as the dosage of lead increased from 10 to 100 ppm, rather than the decrease which would be expected if lead were exhibiting an inhibitory effect.

ACKNOWLEDGMENTS

Special acknowledgment and appreciation for their co-operation and help are due to:

Dr. G. J. Stopps, who suggested the problem and gave valuable advice.

P. E. Smith, Jr., who designed the electrode sets, assembled the Tektronix stimulating and recording units, and gave considerable time to eliminating technical difficulties.

E. F. Fabryka, who made the electrode sets and assisted with the electronic equipment.

C. J. Michaels, Jr., who acted as photographer in several experiments.

Georgina M. Binder, who acted as co-ordinator with events in the autopsy room, noted the crucial times during each sacrifice, and assisted with the calculations.

The personnel in the autopsy room, especially Mary Ann Rubin and A. Stenholm, who provided the amputated hind legs from which the nerves were excised.

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TABLE I

IMPULSE CONDUCTION VELOCITY

Group No.	Lead, ppm, Added to Food	Conduction Distance CMS	N	Average Conduction Velocity ± S.D.* Inflection: m/sec. Males	Inflection: m/sec. Females	Peak: m/sec. Males	Peak: m/sec. Females
RATS OF SPECIAL STUDY: KILLED BY DECAPITATION							
6-Months Treatment. Silicon Oil Used.							
I	0	2.47	9	70±4.9		41±0.7	
		2.97		70±5.1		44±1.5	
II	5000	2.47	10	67±3.9		41±1.6	
		2.97		69±3.2		44±1.8	
I+II		2.47	19	69±4.4		41±1.3	
		2.97		70±4.0		44±1.7	
13-Months Treatment. Silicon Oil Used.							
I	0	2.96	9	73±4.8		45±2.3	
II	5000	2.96	10	70±5.0		44±3.2	
I+II		2.96	19	71±5.0		44±2.8	
RATS OF 2-YEAR FEEDING STUDY KILLED BY CHLOROFORM							
18-Months Treatment. Ringer's Solution Used.							
I	0	2.5	6♂ 6♀	79±7.3	78±6.8	46±3.6	45±2.1
IA	0	2.5	6♂ 6♀	76±7.5	77±4.3	43±1.1	44±2.7
II	10	2.5	6♂ 6♀	71±9.8	71±14.0	43±6.4	44±3.9
III	50	2.5	6♂ 6♀	80±4.7	74±8.4	41±6.0	44±3.4
IV	100	2.5	6♂ 6♀	81±9.7	76±7.4	47±3.8	44±1.8
V	500	2.5	6♂ 6♀	77±7.6	78±5.5	42±1.7	44±2.6
I-V		2.5	72	76±8.3		44±3.6	
24-Months Treatment. Silicon Oil Used.							
I	0	2.97	12♂ 16♀	65±13.7	65±5.3	37±4.9	38±4.1
IA	0	2.97	13♂ 12♀	67±5.8	63±6.0	38±5.6	36±5.5
II	10	2.97	13♂ 16♀	65±7.3	64±4.3	38±3.6	38±3.1
III	50	2.97	12♂ 16♀	65±4.6	64±4.8	36±4.4	39±5.1
IV**	100	2.97	12-13♂ 17♀	64±3.9	64±9.0	37±4.8	37±4.2
V***	500	2.97	0♂ 12♀		63±4.9		37±4.1
I-V		2.97	151-152	64±6.8		37±4.4	

* S.D. - Standard deviation from the mean.

** In one photograph inflection velocity could not be determined.

*** Group V males sacrificed early.

TABLE II

IMPULSE CONDUCTION VELOCITIES: DOG NERVES*

	TREATMENT GROUP AND LEAD ADDED TO DIET				
	I 0	II 10 ppm	III 50 ppm	IV 100 ppm	V 500 ppm
	INFLECTION VELOCITY: METERS PER SECOND				
Male Dogs	78 84 87 92	83 84 87 92	102 98 92 89	99 99 105 93	90 92 93
Avg.	85.1	86.5	95.2	99.0	91.7
Female Dogs	93 87 92 93	84 88 88 98	92 91 89 102	85 93 93 92	91 92
Avg.	91.2	89.5	93.5	90.8	91.5
Males + Females					
Avg.	91.2	88.0	94.4	94.9	91.6
S.D.†	±2.9	±5.0	±5.5	±6.0	±1.1
	PEAK VELOCITY: METERS PER SECOND				
Male Dogs		50 52 50 51	58 50 52 50	57 52 53 51	48 53 52
Avg.		50.8	52.5	53.2	51.0
Female Dogs	53 51 54 52	48 47 52 56	54 53 50 52	50 55 54 52	50 53
Avg.	52.5	50.8	52.2	52.8	51.5
Males + Females					
Avg.	52.5	50.8	52.4	53.0	51.2
S.D.†	±1.3	±2.8	±2.7	±2.3	±2.2

* Kept moist with Ringer's solution during dissection.

† S.D. - Standard Deviation.

TABLE III

F TEST FOR EFFECT OF TREATMENT

	Conduction Distance CMS.	N	Inflection Velocity Avg. Velocity ± S.D.* All Nerves	F	Peak Velocity Avg. Velocity ± S.D.* All Nerves	F
			Meters per Sec.		Meters per Sec.	
Special High Dosage Lead Fed Rats						
6 Month Sacrifice	2.47	19	69 ± 4.4	1.75	41 ± 1.3	0.298
	2.97	19	70 ± 4.0	0.293	44 ± 1.7	0.136
13 Month Sacrifice	2.96	19	71 ± 5.0	1.75	44 ± 2.8	0.358
Rats of The 2-Year Lead Feeding Study						
18 Month Sacrifice	2.5	72	76 ± 8.3	1.35	44 ± 3.6	1.36
24 Month Sacrifice	2.97	151**-152	64 ± 6.8	0.250	37 ± 4.4	0.295
Dogs of The 2-Year Lead Feeding Study						
Males and Females	4.47	33	92 ± 5.6	3.06***	52 ± 2.6	1.22
Males: Groups II - IV	4.47	12	94 ± 7.1	6.62***	52 ± 2.7	0.891
Groups II - V	4.47	15	93 ± 6.4	5.42***	52 ± 2.6	0.748
Females: Groups II - IV	4.47	12	91 ± 5.1	0.596	52 ± 2.7	0.525
Groups II - V	4.47	14	91 ± 4.7	0.442	52 ± 2.6	0.379
Groups I - V	4.47	18	91 ± 4.3	0.393	52 ± 2.4	0.398

* Standard Deviation
** Inflection Velocity could not be determined in one photograph
*** Treatment Effect - Significant at 5% level.

FIGURE 1.

Constant Temperature Shelter With Stimulating and Recording Equipment.

1) Constant Temperature Shelter

2) Telethermometer

3) Stimulus Isolation Unit

4) Recording Unit: amplifier and oscilloscope

5) Tektronix Stimulation Unit

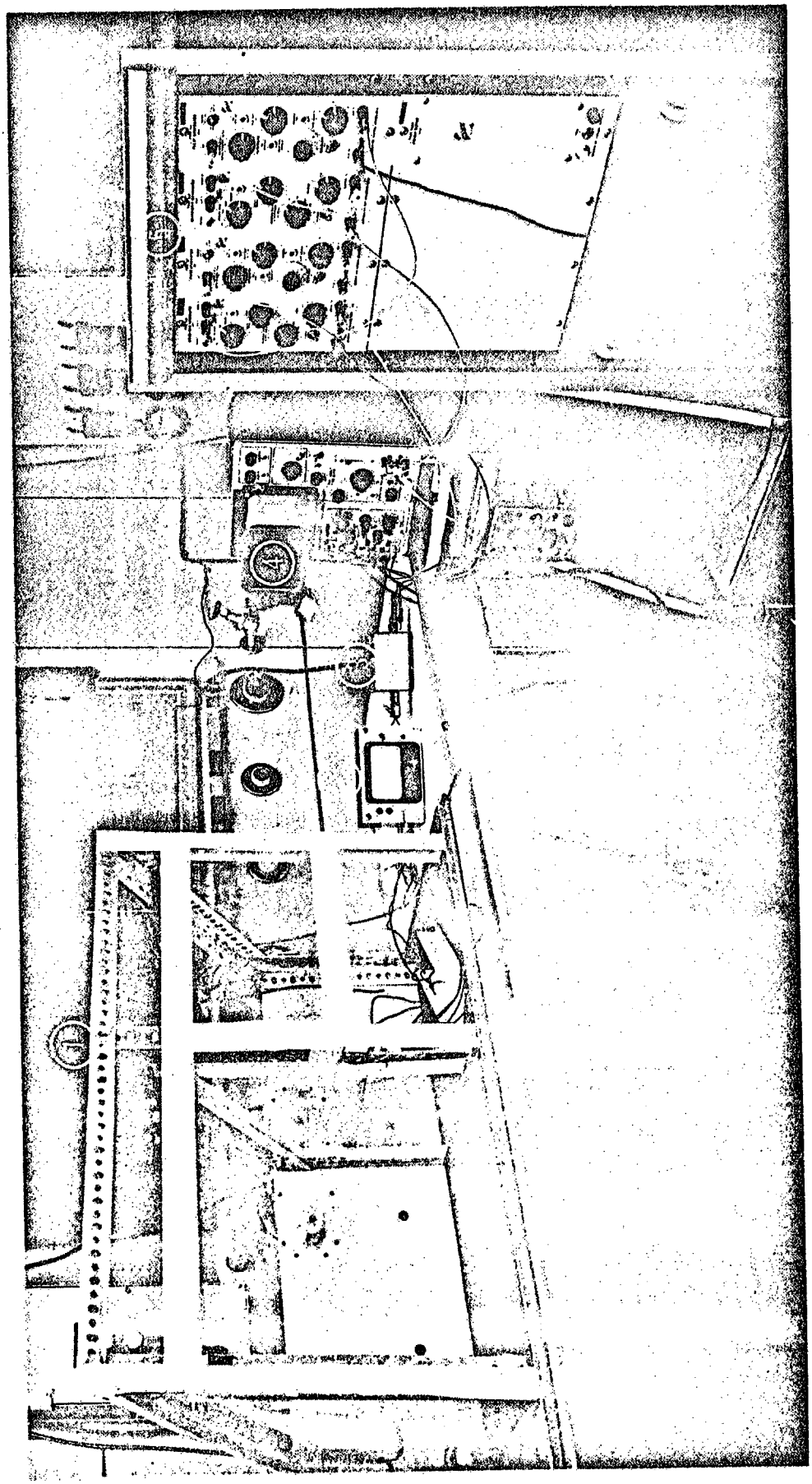

FIG. 1

FIGURE 2.

Large Electrode Set

S_1 S_2: stimulating electrodes

R: recording electrodes

The connection between S_2 and the nearest recording electrode, R, is a ground connection.

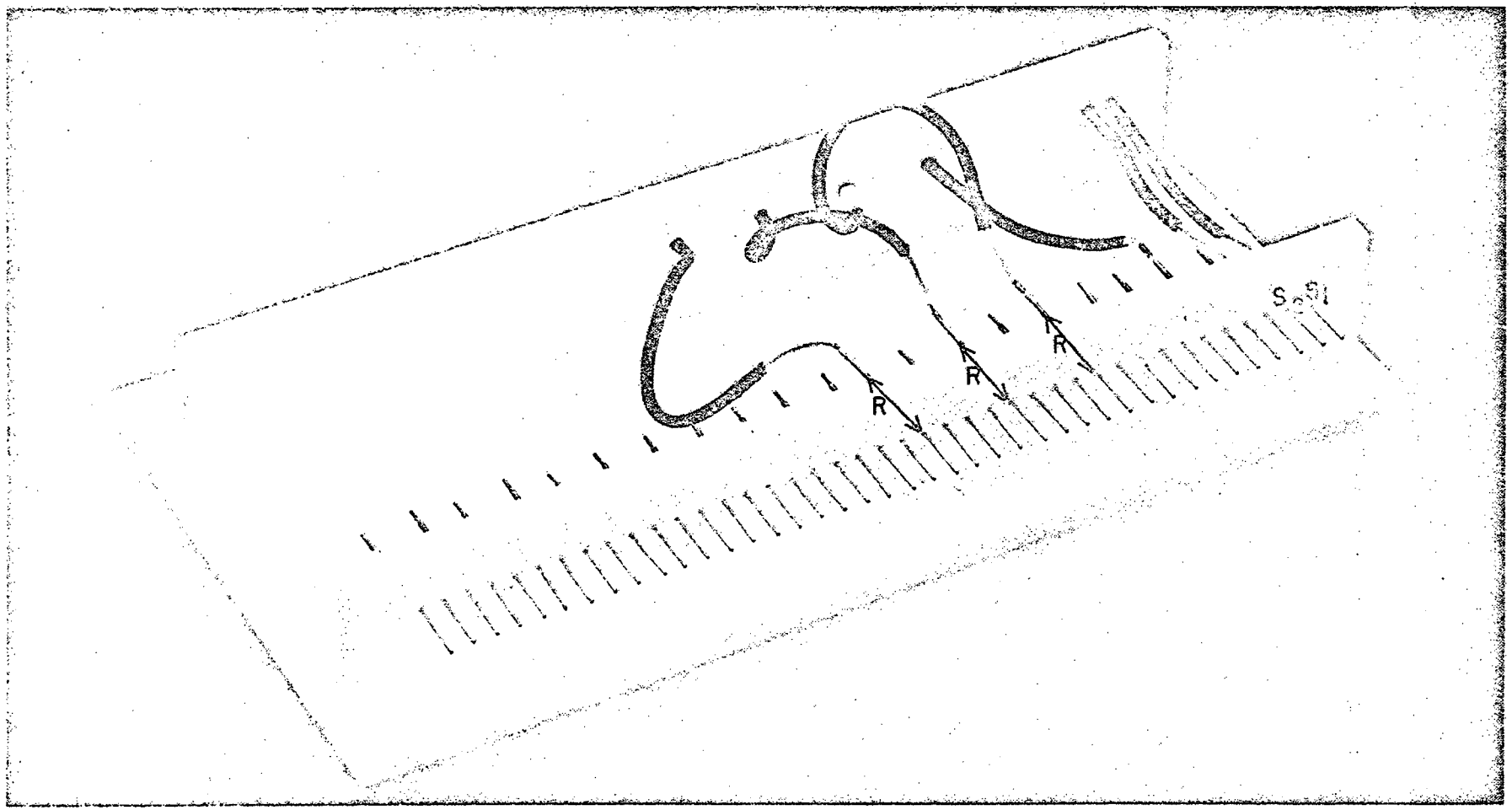

FIG. 2

FIGURE 3.

Tracing, from photograph, of compound action potentials recorded on oscilloscope screen.

Lower Tracing: action potentials recorded as impulses arrive at recording electrode 2.48 cm. from stimulating electrode, S_2.

Upper Tracing: action potentials recorded as these same impulses arrive at the recording electrode 4.48 cm. from S_2.

A: Stimulus Artifact

1: Time Interval between stimulation of nerve at S_2 and the arrival of the most rapidly conducted impulses at the recording electrode 2.48 cm. from S_2, the "inflection".

2: Time Interval between stimulation of nerve at S_2 and the arrival of impulses over the largest number of similar nerves at the same recording electrode, the "peak".

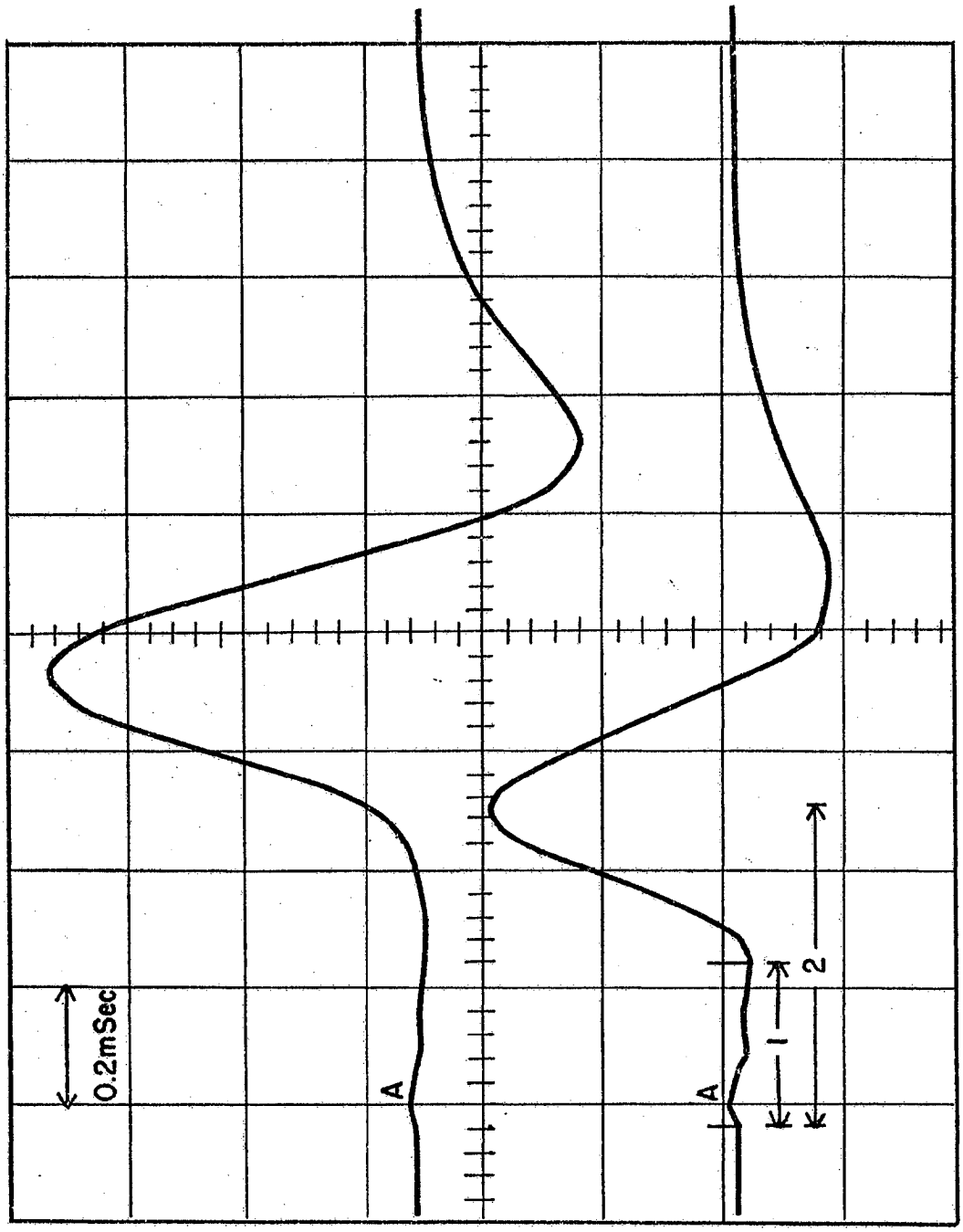

FIG. 3