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

Medical Research Project No. MR-

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" (Hutton, 9 1923). Although today lead-exposed workers seldom develop muscular paralysis (1), any individual with ~~an excessive burden of body lead may be a~~ victim of this paralysis.

The site of this deleterious action of lead on the neuromuscular system has not been definitely established (5, 8). The demonstration of segmental demyelination of nerves from lead-poisoned guinea pigs (5) indicates, however, that the muscular paralysis is ~~at least in part~~ secondary to disturbances in the conduction of ~~nerve~~ impulses ~~to~~ along the nerves which innervate the musculature affected.

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 (11), in many cases of acute polyneuritis (2, 11), which finding may differentiate this condition from acute poliomyelitis (11), and in diabetes mellitus (3, 6, 12, 13, 15, 19). 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 (17) and ten women with

severe polyneuropathy associated with chronic triorthocresyl phosphate poisoning (16). 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* (18). Animal experiments correlate slowed conduction velocity with clinical, and sometimes histological, evidence of nerve damage: in allergic polyneuritis in guinea pigs (10), in diphtheric polyneuritis in cats (14) and guinea pigs (10), 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 conduction velocities of excised nerves, available at autopsy, from the rats and dogs in the 2-year lead feeding study, MR-787.

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 by another electrical contact, the recording electrode,

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

is amplified, and fed into a suitable sensitive 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, 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 tele-thermometer, 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 (Fig. 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.)

* 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.

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 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 4B 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 ~~("pulse out" of wave-form generator of the Tektronix® unit)~~; 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.

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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.

D. Constant Temperature Shelter. During experiments nerves must remain moist; in addition, mammalian nerves must be kept at 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 many 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, provided with a continuous and adjustable supply of warm and moist air, was constructed.

The framework was made with Equipto Type 5700 hot dip galvanized slotted steel, 1 1/2" x 3" x 0.104". The back wall which supports the warm air inlets was made of 1/4" Teflon® sheet, the other walls and the roof of 0.003" Mylar® sheeting. The horizontal dimensions of the shelter are 36" x 18"; its height varies from 24 1/2" in front to 12 1/2" in back, the subsequent slope of the roof providing drainage for the water which condenses on the inner side. Within, a Mylar® partition divides the shelter into a 19 1/2" x 18" "outer" chamber and a 16 1/2" x 18" "inner" chamber. The former has a permanent opening in front and is used for mounting the nerve on the electrodes; the latter shelters the nerve while its action potentials are photographed. A thermistor probe suspended within 4 to 6 centimeters of the 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 109.5°F (43.06°C) dry bulb and 104.5°F (40.28°C) wet bulb, 87% relative humidity, the dry bulb temperature of the inner chamber was maintained at 37.06°C ± 0.4°C.

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 tibialis branch from the rat. During dissection the nerve was protected against drying by the application of a lactated Ringer's solution* (dog nerves and the nerves from the 18-month treatment group of rats of the 2-year feeding study) or by a silicone preparation, † (360 medical fluid, supplied through the courtesy of the Dow Corning Corporation). Nerves which were protected by Ringer's solution The Ringer's - protected nerves were suspended in warm Ringer's solution for 1 - 2 minutes before mounting while those coated with the silicone preparation were mounted immediately or kept temporarily on a spare electrode set within the warm outer chamber.

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 5 to 10 minutes, the larger dog nerves 10 to 15 minutes to adjust to the environment of the inner chamber, As shown by the constancy of the velocity measurements.

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* Cutter's for injection.

†

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 centimeters farther along the nerve. The following discussion applied[5] to either response.

The first small ~~and flat~~ upward deflection lasting 0.5 division (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 and 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, ~~1.25 divisions (0.25 mSec)~~ 0.25 mSec in the lower tracing and ~~2.2 divisions (0.44 mSec)~~ 0.44 mSec in the upper, ~~is the beginning of the~~ there is a large upward deflection which is the compound action potential. After ERLANGER (4) two measurements were made: from the start of the stimulus artifact 1) to the beginning of the upstroke, the "inflection", caused by the arrival of the most rapidly conducted impulses at the recording electrode and 2) to the point of maximum deflection, the "peak", due to the later arrival of the impulses of the largest group of similar fibers. These measurements provide the data for calculation of "inflection" velocity and of "peak" velocity, respectively. In this particular photograph the stimulus artifact was reduced beyond the decrease attainable with the isolation unit by grounding the nerve between the stimulating and recording electrodes ("G", Fig. 2).

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

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 chloroformed. The other 38 rats comprised a special high lead dosage group killed, ~~at the sacrifice of some routine pathological studies,~~ 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:

Average conduction velocities with their standard deviations from the mean are given in Table II.

1. A. Nerves from Decapitated Rats. Inflection velocity, ~~that of the fastest fibers,~~ averaged ~~67-73~~ 67 to 73 m/sec (meters per second), values which overlap those of 71 and 74 m/sec reported by Eliasson for nerves obtained from normal and starved decapitated rats (4). However, peak velocity, ~~that of the largest group of similar fibers,~~ averaged 41 to 45 m/sec, distinctly below his values of 53 to 55 m/sec. The reason for this discrepancy is ~~obscure but may be associated with problems caused by high environmental humidity (see discussion).~~

2. B. Decapitation versus Chloroform. The nerves from the chloroformed rats of the 18-month treatment group had higher, and those from the 24-month group lower, velocities than the nerves from the decapitated animals when comparisons are limited to the values for equal conduction distances. Although the average values do not support the expectation that the chloroform would depress conduction velocity, the large standard deviations which characterize the measurements made on these

nerves indicate that these preparations were not as satisfactory as those obtained from the decapitated rats. However, age, rather than chloroform, could account for the variability since the chloroformed animals were older than the decapitated and many showed gross evidence of degenerative changes.

II. Tibialis Nerves from Dogs:

The data obtained on all the dog nerves are given in Table III. Technical difficulty with stimulation presented satisfactory recordings of the action potential from the nerves from the four male controls. Because of the small number of dogs per group and since a sex difference in the relevant is not obvious, the results for the male and female animals in both sexes because of the small number of dogs per group and since a sex difference is not obvious. The conduction velocities, 84 - 102 m/sec for the fastest fibers and 46 - 58 m/sec for the largest group of fibers, are well within the range for mammalian fibers listed by Grundfest (7).

These dogs were electrocuted, and relatively young; the standard deviations of the average velocities compare favorably with those of the measurements made on the nerves from the decapitated rats.

III. 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 an obvious decrease in velocity due to the 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 IV). Although this test reveals a possible effect of lead on the inflection velocity of the dog nerves,

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

$0.01 < p < 0.05$, the data of Table III are not convincing.

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 ~~chloroformed~~ animals KILLED BY CHLOROFORM.

The preparations from chloroformed animals might be considered unsatisfactory because of the differences in the average values obtained for the nerves from the 18- and 24-month treatment groups and because of the within group variability. However, the nerves from the 18-month group were protected with Ringer's solution during the dissections, the other nerves with the silicone preparation*. When Ringer's solution is used the humidity of the shelter environment must be very high to prevent drying of the nerve; the high humidity introduces recording difficulties which cause an apparent decrease in conduction time so that the calculated velocities are erroneously high (see below). The greater protection afforded by the silicone preparation permits the use of a lower humidity thereby reducing the error. ALSO The reduced velocities of the nerves from the 24-month treatment group could be due to age; decreasing velocity with increasing age has been reported for the nerves of human subjects (3, 12, 13, 15). The within group variations OF THE DATA OBTAINED FOR THE 24-MONTH GROUP might well result from differences in the amount of fiber deterioration and in the amount of damage inflicted by the separation of the nerves from the dense layers of fat in which they were characteristically embedded.

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* The use of the silicone preparation began after the 18-month group sacrifice.

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 above~~ APPROACHES the maximum for the nerve. This apparent shortening of the internal between stimulation and response results in falsely high conduction velocities and the magnitude of the error (velocity increase) depends on 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~~ SYSTEMATIZING THE ERROR BY USING A 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 <u>per se</u>, obvious in the data of Table II, can be eliminated if this distance is standardized.

Variables which, in these experiments, could not be shown to have affected conduction velocity significantly included 1) the dry bulb temperature of the inner chamber which had a maximum variation of 1.1°C 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.

Theoretically, because excitation time is excluded, measurement of the time it takes for impulses to travel the distance between ~~the~~ 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 (Fig. 3) provided velocity values which were so variable that this method of measurement has been abandoned temporarily.

Since all of the nerves obtained during a sacrifice were treated as nearly alike as possible, comparison of the velocities of the nerves from the treated animals with the values of those of the controls killed during the same sacrifice, is valid. Such comparisons do not reveal any interference with impulse conduction which could be considered due to the lead. However, in comparison with nerves of other animal species, e.g. guinea pigs and rabbits, rat nerves have been observed to be resistant to the toxic action of lead (5); the negative results with the rat nerves in these experiments can probably be attributed to this resistance.

No report on the effect of lead on the peripheral nerves of the dog has ~~been noted~~ WAS LOCATED in the literature. Although at the time of autopsy, the three male dogs OF GROUP II had blood lead concentrations ranging from 91 to 114 micrograms per 100 ~~millilliters~~ GRAMS BLOOD and the two females OF THIS GROUP, 52 and 54 micrograms per 100 ~~milliliters~~ grams, concentrations which are considered undesirably high, the dogs appeared healthy and showed no clinical signs of peripheral neuropathy ~~(McGrath)~~.

↓

not in list of refs

CONCLUSIONS

1. Measurement of the impulse conduction velocities of excised nerves obtained from animals at the time of autopsy can provide a functional measurement of the damage inflicted upon peripheral nerve by a toxic compound.
2. Inorganic lead, as lead acetate, administered to rats and dogs in the diet, in concentrations as high as 500 ppm for as long as two years and to rats in a concentration of 5000 ppm for one year, had no significant effect on the conduction velocities of the sciatic-tibialis or tibialis nerves.

Report by: _____

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MEM/dyb

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F TEST = $\frac{\text{Variance due to treatment}}{\text{Variance within groups}}$

F- TEST i) FOR EFFECT OF TREATMENT.

GROUPS II - IV ♂ + ♀ INFL. VELOC F = 4.77 °F FOR COL = 18
°F " TREAT = 2

PEAK " = 1.88 INSIGN.

GROUPS I - IV ♀ only F = 0.48 INSIGN. INFL. VEL. INSIG

= 0.48 PEAK " " "

II - IV ♂ only F = 6.62 INFL. " $0.01 < P < 0.05$

F = 1.44 PEAK PEAK VEL INSIGN.

II - IV ♀ only F = 0.59 INFL. VEL. INSIGN.

F TEST FOR DAY

II - V, F = 1.42 INSIGN INFL. VEL.

0.00 " PEAK "

F TEST, ALL DATA: INFL. SIGN. for treatment at $0.01 < P < 0.05$

	0	10 PPM	50 PPM	100 PPM	500 PPM
♂	—	85.2 m/sec	→ 95.2 m/sec	→ 99 m/sec	[91.7]
		×6.5			
♀		89.5	93.5 m/sec	90.8 m/sec	[91.5]
♂+♀		87.4	→ 94.4	→ 94.9	91.6
		0.01 > P > 0.05			
♂		85.2	95.2	99.0	
		0.01 > P > 0.05			
♀		89.5	93.5	90.8	
		INSIGN			
♀	91.2	89.5	93.5	90.8	
		INSIGN.			

87
87
92
263
87.7

1
83
87
87
92
346
86.5

Dog nerves. f test results

	Infl. vel.		Peak vel.	
MALE + FEMALE. Groups II, III + IV	$f = 4.77$	DF 1 8 2 0.05	$f = 1.88$	1 7 2 INSIG
Females adj Groups II, III + IV	0.59	D.F 9 2 INSIG.		
Males adj Groups II, III + IV	6.55	D.F 9 2 0.05	1.44	D.F 9 2 INSIG
Females adj Groups I, II, III, IV	12/3 0.48	INSIG	0.47	12/3 INSIG

AND THE PEAK VELOCITIES FROM 50 TO 53

4 groups 3/group DF for ctrl. = 12
for treatment DF = 3

REFERENCES

1. Browning, Ethel. Toxicity of Industrial Metals, p. 157; London, Butterworths, 1961.

2. Cerra, D. and Johnson, E. W. Motor Nerve Conduction Velocity in "Idiopathic" Polyneuritis. Archives of Physical Medicine and Rehabilitation 42: 159-163, 1961.

3. Downie, A. W. and Newell, D. J. Sensory Nerve Conduction in Patients with Diabetes Mellitus and Controls. Neurology 11: 876-882, 1961.

4. Eliasson, S. G. Nerve Conduction Changes in Experimental Diabetes. Journal of Clinical Investigation 43: 2353-2358, 1964.

5. Fullerton, Pamela M. Chronic Peripheral Neuropathy Produced by Lead Poisoning in Guinea Pigs. Journal of Neuropathology & Experimental Neurology 25: 214-236, 1966.

6. Gilliatt, R. W. and Willison, R. G. Peripheral Nerve Conduction in Diabetic Neuropathy. Journal of Neurosurgery & Psychiatry 25: 11-18, 1962.

7. Grundfest, H. Bioelectric Potentials. Annual Reviews of Physiology 2: 213-242, 1940.

8. Harvey, S. C. in Pharmacological Basis of Therapeutics, Edition 3; L. S. Goodman and A. Gilman, editors. New York, MacMillan, 1965.

9. Hutton, R. M. Lead Poisoning. Provincial Board of Health of Ontario, Toronto, C. W. James, 1923.

10. Kaeser, H. F. and Lambert, E. H. Nerve Function Studies in Experimental Polyneuritis, pp. 29-35 in Progress in Electromyography edited by P. Pinelli, F. Buchthal and F. Thiebaut, Electroencephalography and Clinical Neurophysiology, Supplement 22; New York, Elsevier, 1962.

11. Lambert, E. H. Diagnostic Value of Electrical Stimulation of Motor Nerves. Ibid, pages 9-16.

12. Lawrence, D. G. and Locke, S. Motor Nerve Conduction Velocity in Diabetes. Archives of Neurology 5: 483-489, 1961.

13. Mayer, R. F. Nerve Conduction Studies in Man.
Neurology 13: 1021-1030, 1963.

14. McDonald, W. I. The Effects of Experimental Demyelination on Conduction in Peripheral Nerve. A Histological and Electrophysiological Study. II. Electrophysiological Observations.
Brain 86: 501-524, 1963.

15. Mulder, D. W., Lambert, E. H., Bastron, J. A. and Sprague, R. G.
The Neuropathies Associated with Diabetes Mellitus. A Clinical and Electromyographic Study of 103 Unselected Diabetic Patients.
Neurology 11: 275-284, 1961.

16. Sala, E. The Motor Nerve Conduction Velocity in Polyneuropathy due to Chronic Triorthocresyl Phosphate Poisoning.
in Progress in Electromyography, pp. 29-35;
Electroencephalography and Clinical Neurophysiology, Supplement 22; New York, Elsevier, 1962.

17. Sessa, T., Ferrari, E. and D'Amato, C. C. Velocita di Conduzione Nervosa nei Saturnii.
Folia Medica 48: 658-668, 1965.

18. Simpson, J. A. Conduction Velocity of Peripheral Nerves in Human Metabolic Disorders.
in Progress in Electromyography, pp. 36-43;
Electroencephalography and Clinical Neurophysiology, Supplement 22; New York, Elsevier, 1962.

19. Skillman, T. G., Johnson, E. W., Hamwi, G. J. and Driskill, H. J.
Motor Nerve Conduction Velocity in Diabetes Mellitus.
Diabetes 10: 46-51, 1961.

FIGURES

Figure 1 - Equipment used in conduction velocity experiments.

1. Nerve shelter. The air inlet to the "outer" chamber (see text) is visible as an inward protrusion of the back wall. The large electrode holder can be seen in the "inner" chamber.
2. Tele-Thermometer.
3. Argonaut Isolation Transformer.
4. Oscilloscope and Amplifier.
5. Tektronix Stimulation Unit.

Figure 2 - Large electrode holder: connected to record from two points along a nerve.

S_1 , S_2 : stimulating electrodes. Conduction distance measured from S_1.

G : ground connection to nerve (any free recording electrode can serve as a ground connection).

R : recording electrodes.

CR : recording electrode: common to both of the recording circuits.

Figure 3 - Copy of "dual" tracing obtained from dog tibialis nerve.

SA : stimulus artifact. Measurements are made from the beginning of artifact.

R_1 : response from recording electrode 2.48 cm from stimulating electrode.

R_2 : response from recording electrode 4.47 cm from stimulating electrode.

I : measurement of conduction time for inflection velocity (lower tracing).

P : measurement of conduction time for peak velocity (lower tracing).

Since deflection magnitude was not measured, each tracing was independently amplified; amplification not necessarily same for both responses.

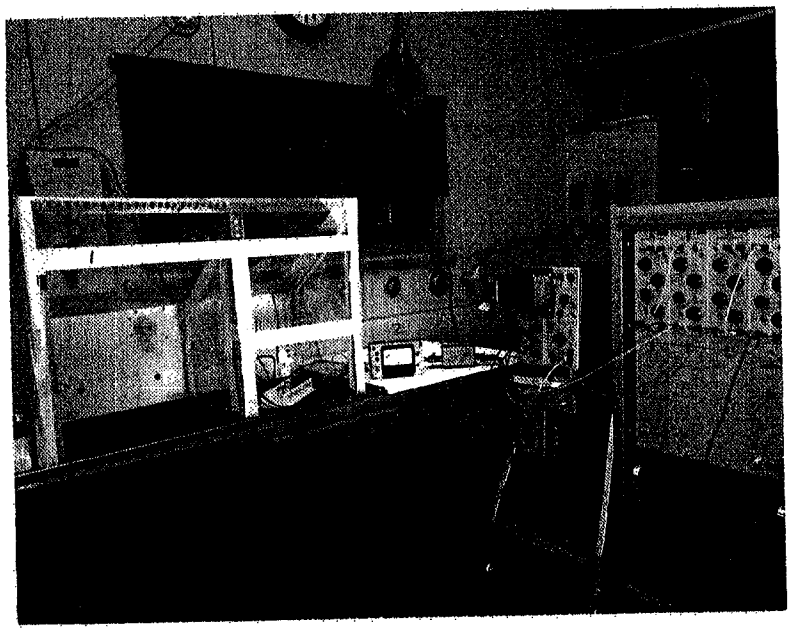
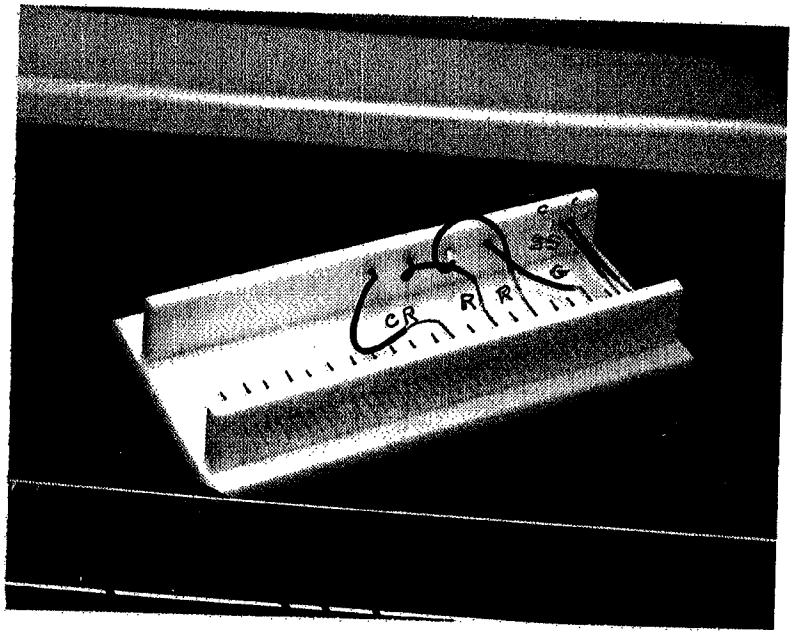


FIG 1



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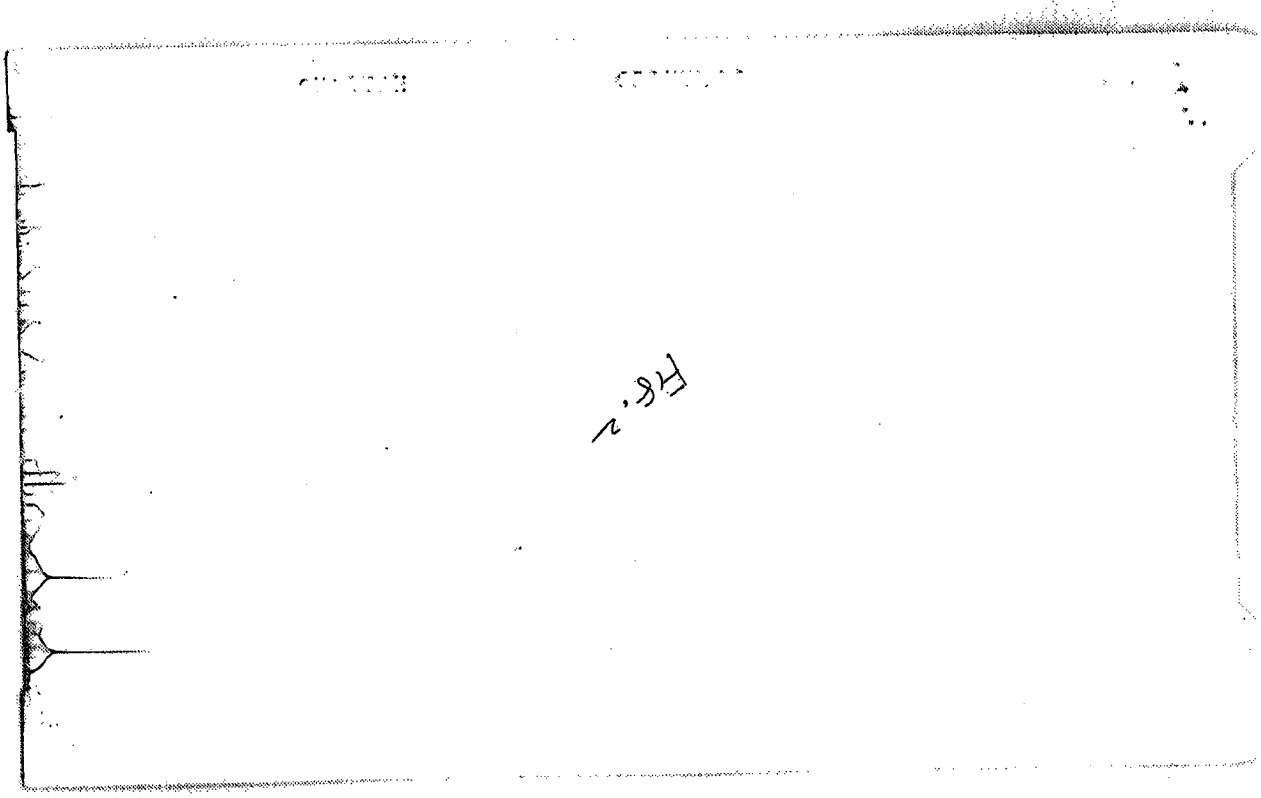
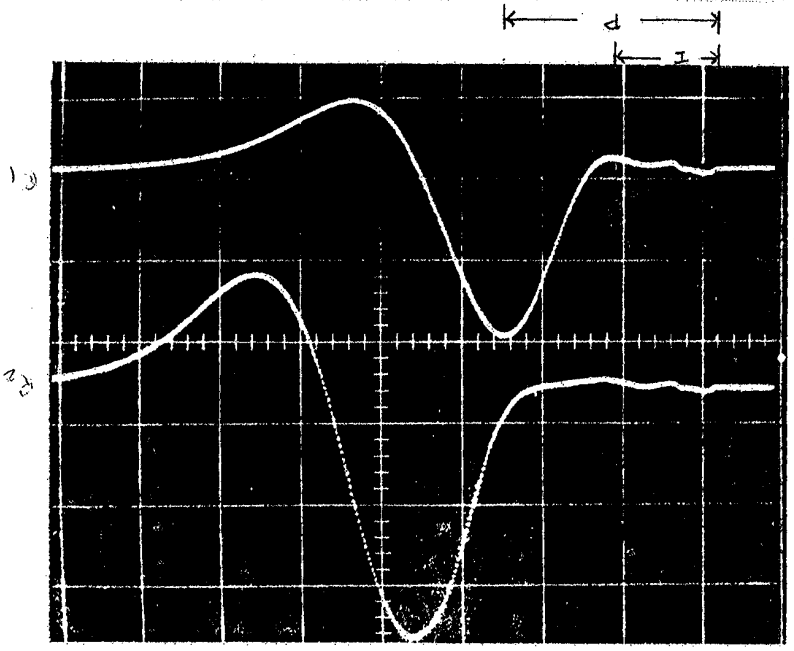


FIG. 2



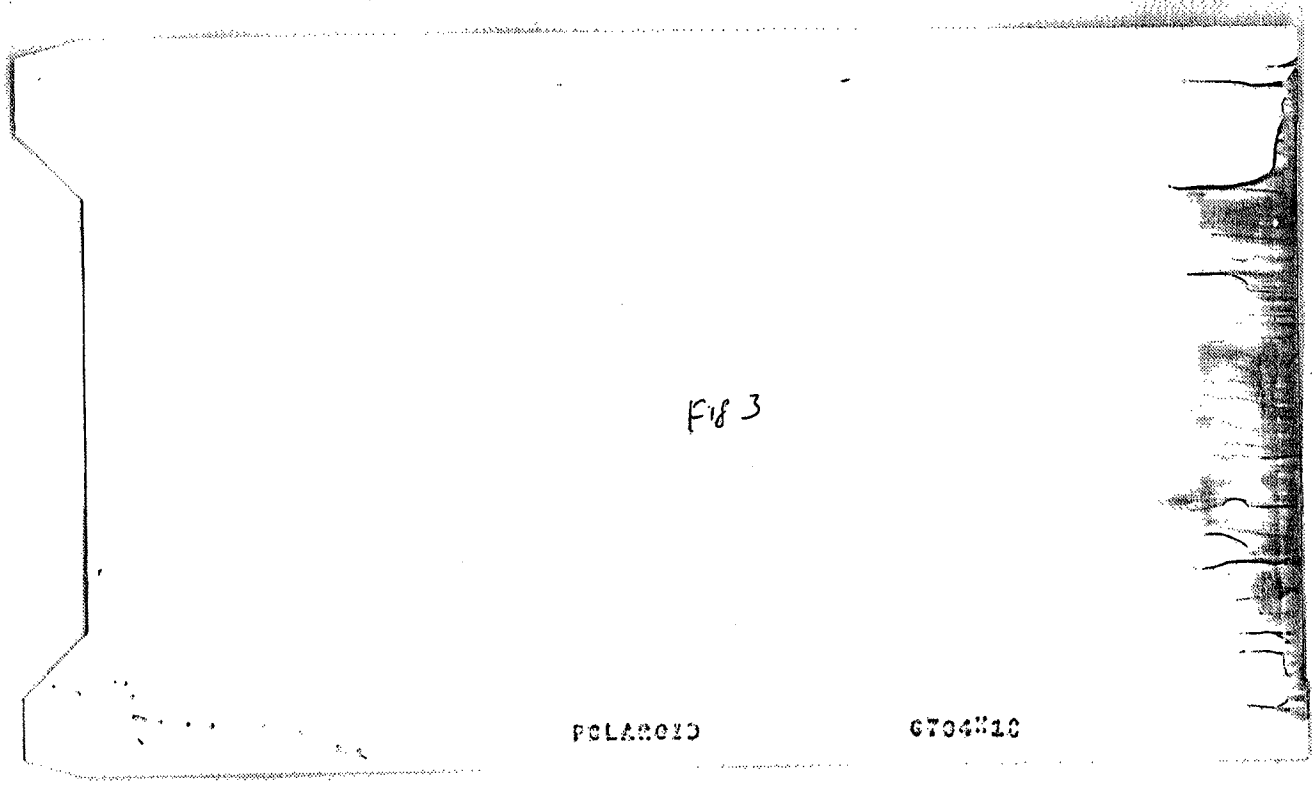


Fig 3

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BOORUM & PEASE "NOTEAR" ®

TABLE I

TWO YEAR LEAD FEEDING STUDY

TREATMENT GROUP	I	IA	II	III	IV	V
LEAD ADDED TO DIET: PPM	0	0	10	50	100	500

DOGS OF 2-YEAR STUDY

NUMBER SACRIFICED AFTER						
1. 24 MONTHS OF TREATMENT						
MALES	*	–	4	4	4	3**
FEMALES	4	–	4	4	4	2**

RATS OF 2-YEAR STUDY

NUMBER SACRIFICED AFTER						
1. 18 MONTHS OF TREATMENT						
MALES	6	6	6	6	6	6
FEMALES	6	6	6	6	6	6
2. 24 MONTHS OF TREATMENT						
MALES	12	13	13	12	12	†
FEMALES	16	12	16	16	17	12

SPECIAL LEAD-FED RATS

TREATMENT GROUP	I	II
LEAD ADDED TO DIET: PPM	0	5000
NUMBER SACRIFICED AFTER		
1. 6 MONTHS OF TREATMENT		
MALES ONLY	9+	10
2. 13 MONTHS OF TREATMENT		
MALES ONLY	9+	10

* NERVES LOST: TECHNICAL DIFFICULTIES WITH RECORDING.

** ONE MALE AND ONE FEMALE SACRIFICED AFTER 12 MONTHS OF TREATMENT. THE SECOND FEMALE DIED [NOT FROM LEAD] ~~ONE~~ MONTH 23.

† MALES SACRIFICED EARLY, NERVES NOT OBTAINED.

\+ ONE CONTROL RAT DIED, ~~ONE~~ NERVE FROM ONE CONTROL

TABLE II.

IMPULSE CONDUCTION VELOCITIES

TREATMENT GROUP	CM. CONDUCTION DISTANCE	AVERAGE CONDUCTION VELOCITIES ± STANDARD DEVIATION			
		INFLECTION: METERS/SEC.		PEAK: METERS/SEC.	
		MALES	FEMALES	MALES	FEMALES
RATS OF SPECIAL GROUP: DECAPITATED					
6 MONTHS TREATMENT					
I	2.47	69.9 ± 4.9		40.6 ± 0.7	
	2.97	70.0 ± 5.1		44.2 ± 1.5	
II	2.47	67.3 ± 3.9		41.0 ± 1.6	
	2.97	69.1 ± 3.2		44.4 ± 1.8	
13 MONTHS TREATMENT					
I	2.96	72.6 ± 4.8		45.0 ± 2.3	
II	2.96	69.8 ± 5.0		44.0 ± 3.2	
RATS OF 2-YEAR FEEDING STUDY; CHLOROFORMED					
18 MONTHS TREATMENT					
I	2.5	79.2 ± 7.3	77.7 ± 6.8	46.0 ± 3.6	45.3 ± 2.1
IA	2.5	76.5 ± 7.5	77.1 ± 4.3	43.4 ± 1.1	43.5 ± 2.7
II	2.5	70.8 ± 9.8	71.4 ± 14.0	43.4 ± 6.4	44.0 ± 3.9
III	2.5	79.6 ± 4.7	74.1 ± 8.4	41.2 ± 6.0	44.3 ± 3.4
IV	2.5	80.8 ± 9.7	76.4 ± 7.4	46.7 ± 3.8	44.4 ± 1.8
V	2.5	76.7 ± 7.6	78.1 ± 5.5	42.5 ± 1.7	44.2 ± 2.6
24 MONTHS TREATMENT					
I	2.97	65.2 ± 13.7	64.9 ± 5.3	36.8 ± 4.9	37.9 ± 4.1
IA	2.97	67.4 ± 5.8	63.3 ± 6.0	37.5 ± 5.6	35.8 ± 5.5
II	2.97	65.1 ± 7.3	63.6 ± 4.3	38.5 ± 3.6	37.6 ± 3.1
III	2.97	65.2 ± 4.6	63.6 ± 4.8	36.3 ± 4.4	38.6 ± 5.1
IV	2.97	64.3 ± 3.9	64.0 ± 9.6	37.1 ± 4.8	37.2 ± 4.2
V	2.97	—	63.4 ± 4.9	—	36.8 ± 4.1

TABLE III

IMPULSE CONDUCTION VELOCITY
DOG NERVES

METERS PER SECOND

	TREATMENT GROUP AND LEAD ADDED TO DIET (PPM)				
	I	II	III	IV	V
	0	10	50	100	500
	INFLECTION VELOCITY				
MALES		78	102	99	90
		84	98	99	92
		87	92	105	93
		92	89	93	
FEMALES	93	84	92	85	91
	87	88	91	93	92
	92	88	89	93	
	93	98	102	92	
N	4	8	8	8	5
AVERAGE	91	87	94	95	92
S.D.	± 2.9	± 5.9	± 5.5	± 6.0	± 1.1
	PEAK VELOCITY				
MALES		46	58	57	48
		52	50	52	53
		50	52	53	52
		51	50	51	
FEMALES	53	48	54	50	50
	51	47	53	55	53
	54	52	50	54	
	52	56	52	52	
N	4	8	8	8	5
AVERAGE	52	50	52	53	51
S.D.	± 1.3	± 3.2	± 2.7	± 2.3	± 2.2

BOORUM & PEASE "NOT

TABLE ~~IV~~ IV

F - TEST FOR EFFECT OF TREATMENT

	N	INFLECTION VELOCITY		PEAK VELOCITY	
		AVERAGE VELOCITY ALL NERVES ± STAND. DEVIATION METERS PER SECOND	F	AVERAGE VELOCITY ALL NERVES ± STAND. DEVIATION METERS PER SECOND	F
SPECIAL LEAD FED RATS					
6 MONTH SACRIFICE					
CONDUCTION DISTANCE 2.47 CM	19	69 ± 4.4	1.75	41 ± 1.3	0.298
CONDUCTION DISTANCE 2.97 CM	19	70 ± 4.0	0.293	44 ± 1.7	0.136
13 MONTH SACRIFICE					
CONDUCTION DISTANCE 2.96 CM	19	71 ± 5.0	1.75	44 ± 2.8	0.358
RATS OF 2-YEAR LEAD FEEDING STUDY					
18 MONTH SACRIFICE					
CONDUCTION DISTANCE 2.5 CM	72	76 ± 8.3	1.35	44 ± 3.6	1.36
24 MONTH SACRIFICE					
CONDUCTION DISTANCE 2.97 CM	151-152	64 ± 6.8	0.250	37 ± 4.4	0.295
DOGS OF 2-YEAR LEAD FEEDING STUDY					
24 MONTH SACRIFICE					
CONDUCTION DISTANCE 4.47 CM	33	92 ± 5.6	3.06*	52 ± 2.6	1.22

* $0.01 < P < 0.05$

§ IN ONE PHOTOGRAPH, INFLECTION VELOCITY COULD NOT BE DETERMINED.