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EFFECTS OF ACCEPTABLE LEVELS OF LEAD ABSORPTION ON HUMAN

PERFORMANCE IN RELATION TO BIOCHEMICAL AND NEURO-

PHYSIOLOGICAL CHANGES

by

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Thesis presented under General Regulations for the

Degree of Ph.D. in the University of London.

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March, 1978.

ABSTRACT

The ability of workers exposed chronically to lead to perform a number of performance tests has been related to their neurophysiological and biochemical changes.

A group of 97 workers exposed to inorganic lead and 109 matched controls were selected from two battery manufacturing plants. The stratification of labour in terms of ability and cleanliness of job was considered to be minimal in these factories; such stratification could lead to apparent drop in performance with increasing blood lead values if less demanding jobs in terms of ability are associated with increased lead exposure.

The exposed and control subjects were tested for adding ability, reaction time, grip strength, endurance, tapping speed, eye-hand co-ordination, tremor and nerve conduction velocity; blood and urinary lead and amino-levulinic acid in urine were measured. Information on clinical subjective symptoms, smoking and drinking habits was also obtained.

Over a blood lead range of 13-79ug/100ml. no indication of a dose response relationship in exposed and control groups was found for performance tests, motor nerve conduction velocity, lead and amino-levulinic acid in urine.

A reduced statistically significant motor nerve conduction velocity has been found for the group of exposed workers in one factory, but not in the other. The changes observed in motor conduction velocity appear to be of no significance in terms of workers' biochemical and performance parameters.

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ALA - d-amino levulinic acid

ALA-D - d-amino levulinic acid dehydrase

CP - Coproporphyrin

ECG - electrocardiogram

EDTA - ethylene diamin tetra acetic acid

EMG - electromyography

IQ - intelligence quotient

MMCV - maximum motor conduction velocity

MS - maximum slope

PBG - porphobilinogen

REM - rapid eye movement

RT - reaction time

SH - sulphidril group

UPG - uroporphyrinogen

4. ACKNOWLEDGEMENTS

Grateful acknowledgements are made to the following:

PROFESSOR R.S.F. SCHILLING for giving me the opportunity to do this
Ph.D. in T.U.C. Institute of Occupational
Health, Great Britain and for advice
throughout the whole project.

MR. G. CROCKFORD, Senior lecturer in Occ.Hygiene, for invaluable
assistance, advice and discussion throughout
the whole project, also for being a willing
volunteer for the tests.

DR. J. TAYLOR and MR. R. HIGGINS and DR. M. WILLIAMS, from Chloride
Automotive Batteries Ltd. for permission
to carry out the project at their factories
and for their hospitality throughout
the investigations.

MR. E. KING and Staff of the National Occupational Hygiene Service
for performing the biochemical tests.

DR. P. LEQUESNE and DR. M. HARRISON from Middlesex Hospital for
performing the nerve conduction velocity tests
in the second battery factory.

MISS J. WALFORD, statistician, for invaluable help in analysing the
data.

SISTERS E. SMITH and S. RAINFORD from the medical departments of both
factories for collecting the biological
samples and for organisation and help.

COMMANDER D. DAVIS from the Royal Navy Environmental Medicine Unit
for lending the tremor equipment.

The Management and men of Chloride Industrial Batteries Limited,
Manchester and Dagenham, for allowing me to
carry out the tests, for volunteering for testing
and for their kind hospitality.

MR. JOHN HUGH, MR. E. KING and MR. D. DALLOW for building and validating
some of the electronic equipment used in
the project

MR. JOHN STIFF for his kind assistance in typing this thesis.

To all staff of the T.U.C. Institute of Occupational Health who gave me
help and encouragement and who volunteered as
subjects for the performance tests.

5. INTRODUCTION

Among the heavy metals, lead is probably the most important as
a toxic hazard to man: it is an insidious element in our environment
and can accumulate in the body with no noticeable effect until it
produces a serious loss of health.

Since antiquity, lead poisoning has been known due to the wide
use of the metal in many different industries.   Today there is no
reason why fatal or very severe lead poisoning should occur (Newhouse,
1976), and the main cause of concern is the effect of small quantities
of lead in the environment on the whole community.

The study of behavioural toxicolgy has changed the classic view
of lead poisoning and enables subclinical lead posoning, which according
to Waldron and Stöfen (1974), may be defined as the production of
morbidity or mortality without the appearance of the classical signs
and symptons of clinical lead poisoning, to be investigated.   Behavioural
toxicology which combines the resources of the experimental toxicologist
and psychologist, measures the subclinical but possibly still deleterious
effects of lead on the central and peripheral nervous system.

The present project on the subclinical effects of inorganic lead
uses the techniques of behavioural toxicolgy and was carried out in two
stages: firstly, a study which assessed some performance tests for
detecting behavioural changes in lead-exposed workers, and which has
already been reported (Milburn, Mitran and Crockford, 1976).   Secondly,
the present study which extended the number of performance tests and
correlates their results with neurophysiological and biochemical
studies.

The performance tests used were selected to provide similar
batteries of tests to those used by Chaffin and co-workers (1973), for

testing the behaviour of workers exposed to mercury. A questionnaire was also designed to elicit information of subjective nervous psychological, visual and gastro-intestinal disturbances associated with the clinical symptoms of inorganic lead poisoning.

The neurophysiological studies performed were, maximum motor conduction velocity for median and ulnar nerves of dominant hand, and the percentage of amplitude of muscle action potential elbow/wrist. The biochemical tests included blood lead, urinary lead and ALA.

6. REASON FOR THIS RESEARCH

Man is exposed to many toxic pollutants both at work and in the general environment; one of the most important of these pollutants is lead. There is evidence that the currently accepted levels of lead exposure in the lead industries does not produce mortality (Lane et al, 1968), and the experience of industrial medical officers, management, unions and shop-floor workers provides subjective evidence that other adverse health effects do not occur. This subjective evidence is undocumented, and could be faulty or biased. Not so subjective, however, are the changes in nerve conduction velocity which have been observed in lead workers. It is important to recognise that changes in bodily function or biochemical parameters do not necessarily represent damage or pathological changes as they may be adaptive in nature (Dinman, 1972). It is therefore important to determine the significance of changes in physiological and biochemical parameters in terms of the altered performance of specific tasks, the tasks being selected as far as possible to demonstrate the particular injury caused by an environmental pollutant.

Although the determination of the levels of exposure at which
damage to health occurs, as indicated by decrements in the performance
of tasks is of primary importance, it is also important, in view of
public concern and pollution control policy, to demonstrate that up
to a certain level of environmental contamination, a pollutant does
not affect in any detectable way the health and performance of adults,
nor the development of children, although detectable adaptative
biochemical and physiological changes may be demonstrable.

Consequently, in this study, negative findings are as important
as positive ones, and an attempt will be made to distinguish between
potentially pathological changes, if any changes are found, and
adaptive changes. This will require very careful assessment of the
performance, physiological and biochemical tests, to determine their
sensitivity and resolving power. Among the heavy metals, lead has
been selected for investigation as it has known effects on the nervous
system, and produces a reduction in the conduction velocities of small
nerve fibres before there are any clinical signs of lead exposure
(Seppalainen, 1975). A number of recent studies indicate that workers
with elevated blood levels show a slowing of motor nerve conduction
velocity (Seppalainen and Hernberg, 1972, Feldman et al, 1977).
These changes in nerve conduction velocity could affect or be
associated with alterations in the performance of psychomotor tasks
such as reaction time. Other workers have studied performance
(Hernberg, 1973) and found it to be affected; likewise subjective
symptoms have been studied and found to be associated with lead
exposure. Many of these studies have been performed on men with
very high blood lead levels or a history of lead poisoning, and

undoubtedly decrements in wellbeing, performance and health are to be expected. The problem confronting the research worker is one of defining the point below which adverse changes in health performance and wellbeing are unlikely to occur.

The first aspect to be considered is whether changes in a measured biochemical or physiological parameter lie within the normal range maintained by homeostatic mechanisms or not (Waldron, 1974), and if they do, is there a more restricted range beyond which there may be an undesirably large demand on the organisms available energy which could, over a period of time, affect its general wellbeing (Zielhuis, 1974). In considering this point, it is well to remember that with regard to the capacity of some physiological functions, the body has a surplus of capacity, e.g. ventilatory capacity for exercise. The same appears to be the case with nerve conduction velocity - changes in motor nerve conduction velocity of six metres per second occur naturally as a result of changes in nerve temperature. The range of peroneal motor conduction velocity, for example, found in the 20-30 year-old population spans 45-55m/sec. and a change of similar magnitude occurs between the ages of 20 and 60 years (Archibald, 1976).

The reported decrements of about 2 m/sec. in nerve conduction velocity in lead workers would therefore appear to be of little significance, particularly as the work of Seppalainen et al (1975) has shown that nerve conduction velocity remains stable after an initial drop during the first few months of exposure, so indicating that homeostatic mechanisms may be involved. However, a study of lead workers by Repko et al (1974) has indicated that changes in performance do occur in populations exposed to lead, and that changes can be correlated with blood lead levels when they are in excess of 70 micrograms/100ml. of blood. The problem with this type of study is

that selection or stratification of the labour force may occur in the factories, the less able people finding themselves doing the dirtier, less desirable jobs. At the same time, those who find themselves in the dirtier jobs may observe less demanding standards of hygiene with a consequent increase of blood lead level. Tests of psychomotor performance on such populations may therefore not only identify effects due to lead as such but job selection in terms of the worker's ability. The effect of selection can possibly be ignored at high levels of blood lead, but at about the threshold level, where evidence is being sought for setting an environmental standard, it becomes of crucial importance. It is most important to identify the true threshold and not a pseudo-threshold which is a property of the exposed population.

7. BACKGROUND TO INORGANIC LEAD

7.1 Generalities and its use in industry

Lead occurs naturally as the sulphide galena which is usually combined with the sulphides of other metals such as: silver, arsenic, bismuth and cadmium.

The lead compounds obtained from galena are:

- Litharge (PbO) named "massicat".
- Red lead (Pb_3O4) - the higher oxide of lead called "minimum".
- White lead - basic carbonate hydrate ($2PbCO_3\ Pb(OH)_2$)
- Lead chromate and basic lead chromate ($PbCrO4$ and $PbOPbCrO4$)

Lead also occurs naturally as cerussite ($PbCO3$) and anglezite ($PbSO4$). Metalic lead at usual temperature is covered by a fine layer of lead oxide. In Great Britain the most important inorganic

forms of lead are the oxides used for batteries, lead cable sheathing, sheet, pipe and alloys of various types. Other lead compounds are used as additives in gasoline and lead pigments of various types in the manufacture of plastics, glasses and glazes. The pattern of lead usage is much the same in the main industrial countries and the metallic uses have tended to increase more than those of most lead compounds, except lead additives for gasoline.

The severity of the inorganic lead hazard in the various processes has been estimated by Elkins (1959). From the result of investigations by himself and his associates he considers that the most severe hazard occurs in the spraying of molten lead and lead paint; in the grinding or power sanding of lead or solder; the pouring of leaded iron and steel; in certain operations in storage battery manufacture; the operations of wire patenting; the mixing and weighing of lead powders. Lead smelting and burning are also sources of harmful exposure, while soldering lead casting, brush painting, linotyping and steel tempering are regarded as relatively non-hazardous -(Browning, 1969).

Because the present study had been carried out on groups of workers exposed to inorganic lead in the storage batteries factorires, the type of hazard involved in this industry will be briefly described.

The manufacture of electric storage batteries may involve a substantial lead exposure, as has been shown by Cantarow and Trumper (1944) and Gibson et al (1968). The essential component of a storage battery is a plate, consisting of a lead grid which serves to hold the active lead peroxide material (positive plate). Lead grids and balls are processed in a "ball mill" with formation of a mixture of lead and lead oxide. The mixture is moistened with

sulphuric acid to form the paste which is applied to the grids. After
drying the plates are connected to their proper position in weak
sulphuric acid. The negative sponge lead and positive lead peroxide
are then formed by transmission of electric current. This process
is called forming. After forming, the plates are again dried. After
some finishing operations they are ready for assembly. Here the
plates are brought together in their desired groups, burned together
and placed into cells. The battery is then ready for the final charge.

In addition to the workers engaged in the manufacturing process
itself, there are workers in a battery factory who do various kinds
of jobs such as stoking, reprocessing work and truck driving. These
workers spend part of their working time in the lead contaminated
environments of the factory.

It is generally accepted that exposure to inorganic lead or its
compounds can be safe provided that the average concentrations in
the air is kept below the Threshold Limited Value (TLV). At present
the recommended level is 0.15 mg/m^3 for lead and it's compounds (except
tetraethyl lead) in the U.S.A. (Criteria for recommended standard 1972).
Several Western European countries, including Great Britain, West
Germany and Finland have adopted this value. In Sweden, a lowering
of the TLV to 0.1 mg/m^3 is under consideration (Hernberg, 1973).

These standards are time weighted average exposures for eight
hours a day, 40 hours a week, for a working lifetime. Socialist
countries in general have recommended lower values, since they base
their standards upon other norms. Thus the M.A.C. for the Soviet
Union is 0.01 mg/m^3, that for Hungary 0.02 mg/m^3 and that for Poland
and Czechoslovakia 0.05 mg/m^3 (Hernberg, 1973b). Romania has M.A.C.
for inorganic lead of 0.1 mg/m^3.

7.2 Lead in the General Environment

Lead is one of the most abundant metals known to mankind and the industrial products containing lead are widely distributed in the environment. The current world consumption of refined lead is about four million tons/year, and has grown during the past decade at an average rate of 3.5 per cent/year.

7.2.1 Lead in Soil

Lead in soil levels depends to a great extent on geographical location and on the uses to which the soil has been subjected; no soil however, has been found to be completely free of lead. Virgin soils contain the lowest concentration of lead, but the range is wide and depends on the type of soil. The average lead content of the earth's crust is 16 p.p.m. and the usual range 2-200 p.p.m. (Waldron and Stofen, 1974). Thompson (1969) reported that the highest concentration of lead in soils is found near natural deposits of lead (20-19,000 p.p.m.) or near sites where lead has been used for industrial purposes (17-40,175 p.p.m.).

There appears to be a natural mechanism by which lead tends to be moved upwards in the earth's crust, so that a sharp lead profile with higher values at the surface than in the deeper layers is frequently found. Swaine and Mitchell (1960) in a study of lead profiles of eight soils in Scotland found that lead content was approximately halved in going from the surface to a depth of 50 inches. Wright et al (1955) reported a similar result in four virgin soil groups in Canada. Soils in both studies were from uncultivated areas.

The concentration of lead in the street dust and surface soil of large cities is extremely high. In a study of 77 mid-western cities ranging in population from 100,000 to 1,000,000, the average concentrations of lead in dust collected from residential and

commercial sites were 1,636 p.p.m. and 2,413 p.p.m. respectively -
(National Academy of Sciences, 1972). Giubileo (1957) found the
concentration of lead in the street dust of Milan to be 1,360-2,360
p.p.m. in central streets, and 800 p.p.m. in peripheral streets.
Waldron and Stofen (1974) cited Stephens (1972) who found that the
highest value in the street dust in Birmingham was >5,000 p.p.m;
also he found that house dust may contain high levels of lead.

7.2.2. Lead in Water

The lowest concentration of lead in water occurs in sea water
and varies from 0.00008 p.p.m. to 0.02 p.p.m., whilst that of fresh
water from streams is in the range of 0.0001 p.p.m. to 0.006 p.p.m.
(Thompson, 1969). He also showed that the lead content in drinking
water ranges from 0.03 p.p.m. to 0.5 p.p.m. The range of lead
concentrations in drinking water after it had been allowed to stand
in lead pipes for two days was found to be 0.37 to 0.92 p.p.m.
due simply to the dissolution of lead pipes by the water.

In Great Britain the lead content of drinking water ranges from
0.019 to 0.025 p.p.m. in towns with a soft water supply, and 0.023
to 0.033 p.p.m. in towns with a hard water supply - (Thompson, 1969).
It is now appreciated that the lead concentration of domestic
water supplies can be significant, particularly in soft water areas
where the plumbing systems are made of lead, especially lead storage
tanks for drinking water.

Beatty et al (1972) found a direct correlation between the level
of lead in the drinking water and the level of lead in the blood and
an indirect correlation with the level or erythrocyte ALA - dehydratase
in the inhabitants of the householders in the Glasgow area. This
urban survey did not define any clinical abnormality attributable to
these elevated blood lead levels. However, in a study of long standing

exposure to drinking water of high lead content, there was frank
lead poisoning in some cases. The recent findings of Meredith et al
(1975), that soft water in comparison to hard water is associated with
an increased absorption of lead in experimental animals is another
factor which must be taken into consideration.

In rain water the level of lead varies due to dust contamination.
From samples collected near a busy motorway in Cincinatti, lead
varies from 0.1 to 0.49 mg/litre. Slow rainfall is more effective
in removing lead from the atmosphere and rain water contributes
little to the total lead content of the soil. It is estimated that
the rain fall contribution is only about 1 ug. per cm-rain per year,
(National Academy of Sciences, 1972).

Thompson (1969) mentioned the levels of lead in snow and reported
that those of Antartic snows were less than those found in Greenland
by a factor greater than ten. It is now approximately 0.2 mg/kg.
in the recent snow.

7.2.3. Lead in air

Lead in the atmosphere is generated mainly by petrol propelled
vehicles and by lead industries especially the smelting of lead ores.
Emissions of lead from smelting industries are small in comparison
with the emissions from burning gasoline. The inorganic emission
from the combustion of leaded gasoline constitutes approximately 98%
of the total emission of lead from listed sources.

The chief inorganic forms of lead products in the atmosphere are:
Lead bromochloride (PbCl - Br), Alpha and Beta forms of ammonium
chloride and lead bromochloride (NH_4 Cl 2Pb Cl Br 2 NH_4Cl Pb Cl Br)
lead sulphate (Pb SO_4) mixed lead oxides and lead hilaides. The
sources of lead emissions into the atmosphere are shown in Table 1.

Table 1.   Lead emission in U.S.A.

Emission Source	Lead emitted, tons/year
Gasoline combustion	181,000
Coal combustion	920
Fuel oil combustion	24
Lead alkyl manufacturing	810
Primary lead smelting	174
Secondary lead smelting	811
Brass manufacturing	521
Lead oxide manufacturing	20
Gasoline transfer	36
TOTAL	184,316

(from 'Lead' - Academy of Sciences,1972)

The other sources of atmospheric pollution, which have not been included in the above table are:

Exhausting workroom atmosphere.

The abrasive action of automotive traffic on lead painted line dividers on streets and highways.

Resuspension of lead by high speed cars.

Burning of lead, painted surfaces of houses, bridges and other structures before repainting.

Welding of lead painted structural or other steels.

Weathering of painted surfaces with the resulting flaking and distribution in the atmosphere of a portion of the lead-bearing dust.

Incineration of leaded plastics and other materials whose usefulness has ended.

Recovery of lead from old battery cases, lead pipe, lead
sheathed cable and sheet lead in secondary smelters.

The welding and soldering operations conducted via plumbing
and electrical repair shops.

The magnitude of these sources could be very important, but at the
present is unknown (National Academy of Sciences, 1972).

7.2.4. Lead in plants

Lead may enter plants either by their root system or through
foliar uptake. Bazzaz et al (1974) found that lead and cadmium
inhibit photosyntheses and transpiration of sunflower and corn leaves.

The contamination of vegetation growing along highways decreases
the further they are from the road (Warren, 1974). This was confirmed
by Motto et al (1970), who studied the lead content of five crops grown
in three field at varying distances from highways. Those plants
growing closest to the highways had the highest lead content. The
distribution of lead in these plants was different from plants grown
inside a greenhouse in leaded soil or sand. The crops in the field
contained most lead in the aerial parts whilst those grown in the
leaded soils had most lead in the roots. These results indicated
that plants may take up lead both by their leaves and roots, but that
relatively little translocation takes place within the plant, although
Mitchell and Reith (1966) did observe the translocation of lead from
root to shoot in rye grass during the winter period. Waldron and Stofen
(1974) have shown that trees have doubled their lead intake in the
past thirty years.

Plant species vary considerably in their lead contents. In Great

Britain, lead arsenate is rarely used as an insecticide, and then only on apples and pears, with a minimum interval of six weeks between application and harvesting or on non edible crops (Waldron and Stofen, 1974).

For vegetation near busy highways in Britain the evidence does suggest some contamination by lead derived either directly from exhaust fumes or from contaminated dust. The effect is largely one of surface deposition with the outer leaves showing more lead than the inner leaves. Thus for crops growing near the Great North Road in 1964, the lead content (p.p.m. oven dry material) fell from 5.0 at 10 yards to 1.0 at 150 yards from the highway for outer leaves and from 1.0 to 0.4 for inner leaves (Hepple, 1972).

The range of lead content in different types of vegetable food is very wide. Kehoe (1933) found that the range of concentration in cereal was from 0.03 to 0.31 p.p.m., Warren and Delavault (1962) found it to be from 0.3 to 7.0 p.p.m. but added that many of the samples were either subjected to lead pollution or were grown in soil with an abnormally high lead content. In various legumes lead was found to be from 0.03 to 0.3 p.p.m (Kehoe, 1933).

The lead content of fruit varies widely according to different authors. Kehoe et al (1933) found the range to be 0.04 to 0.18 p.p.m. whereas Monier-Williams (1950) gives values in the range of 0.2 to 0.9 p.p.m. for various sorts of fruit. This variation might partly be explained by the use of lead arsenate as an insecticide. The fact that this contributes to the concentration of lead in some fruits was shown by Thompson (1969), who found that the core and peel of apples

imported from Australia in 1963/64 contained more lead, on average
3.45 p.p.m. than the flesh, 0.5 p.p.m. As other insecticides have
replaced lead arsenates, the lead content of apples from Australia
has decreased so that in 1964/65 the average lead content of the peel
and core was 1.55 p.p.m. and that of the flesh 0.1 p.p.m. The lead
content of various vegetable foods then may not be solely due to
the natural presence of lead in tissues, but may derive partly from
surface contamination.

Warren (1974) compared the lead content of trees growing in a
rural area of Sussex with those growing in London and found that the
locality influenced the lead content to a great extent; the trees
growing in London contained over twenty times more lead (20 p.p.m.)
than those growing in Sussex (0.8 p.p.m.). He attributed this to a
higher atmospheric lead content in London which in turn was attributed
to a greater volume of traffic. Lead found in the vegetable tissues
derives from the soil in which the plant is growing and also from the
water it takes in, also partly from the atmosphere in the course of
respiration and phtosinthesis, but the major part of the lead content
which Warren found in London trees is probably caused by contamination
of the leaf and stem surface by dust and exhaust fumes.

8. LEAD METABOLISM

8.1 Definitions of lead poisoning

Occupational exposure to inorganic lead occurs mainly through
inhalation of dust, although ingestion and skin absorption may also

play a substantial role. The general population may be exposed via air, water and food, and smoking could play an important role.

Regarding the stages of lead absorption, a clear distinction is often made between lead absorption and lead poisoning (Browning, 1969). In lead absorption without any symptoms there may be a mild anaemia, punctate basophilia and reticulocytosis, an increase in lead content of blood, urine and faeces, and of coproporphyrins in the urine. Gibson et al (1968) refers to the difficulty in determining at what point a state of exposure to lead merges into a state of toxicity.

Waldron (1971) defines lead absorption as the uptake of lead by the subject from his environment by any route and lead intoxication (pharmacological or chemical) as evidence that absorbed lead is interfering with some metabolic process in the body. This appears to make absorption identical with intoxicati n in the light of evidence of interference with haem metabolism by very small amounts of absorbed lead. As it is no longer possible to maintain a clear division between absorption and poisoning it might be better to abandon the effort.

The use of biochemical tests has shifted the diagnostic emphasis in such a way that it might be preferable to talk of lead in terms of its chemical toxicity without symptoms, and its chemical toxicity with symptoms - the one merging into the other as a continuous process (McCallum, 1972).

At an International meeting on the Toxicology of Metals (Nordberg, 1976), a new conceptual consideration on heavy metals has been suggested such as: critical organ, critical concentration in cells and

organs, critical effect, dose-effect and dose-response relationship.
The following is a brief review of these concepts.

Critical Organ is defined as that particular organ which first
attains the critical concentration of a metal under specified
circumstances of exposure and for a given population. The organ of
greatest accumulation is not necessarily the critical organ e.g. in
the lead exposure the highest concentrations may be reached in bone
without any identifiable effect; the bone is therefore not the
critical organ.

Critical Concentration for a cell is the concentration at which
undesirable functional changes reversible or irreversible occur.
The lethal concentration for a cell was defined as the cellular
concentration sufficient to cause the death of the cell.

Critical Organ Concentration was defined as the mean
concentration in the organ at the time any of its cells reaches
critical concentration. The critical organ concentration may be
considerably higher or lower than the critical concentration for a
particular cell. This is possible since the type of cell that first
attains the critical concentration is not necessarily the type of cell
with the highest concentration.

Since there exist biological variation in sensitivity among
individuals, a certain inter individual variation is to be expected
also in critical organ concentrations.

The critical organ concentration may even be subject to
variation both in an individual and in a population.

Critical effect is connected with the critical organ, the organ
that becomes critical may vary depending on the characteristics of the

population exposed. There is some evidence that in children exposed to lead, the brain may be the critical organ, whereas this is not necessarily the case for adults.

So, the point at which an adverse effect is present, the relationship between dose and effects in the individual, represent the critical effect. This critical effect may or may not be of immediate importance for the health of the whole organism.

Subcritical effects are defined as the exposure level that is lower than the one giving critical concentration of metal in the critical organ. Some effects might occur that do not impair cellular function but are still evident by means of biochemical or other tests. In lead exposure, inhibition of the enzime amino-levulinic acid-dehidratase (ALA-D) in the cells of bone-marrow is a subcritical effect which precedes an increased level of ALA in blood and urine and the occurence of anaemia (critical effects). A decrease in ALA-D activity in blood is an example of an indicator of a subcritical effect of lead exposure.

The term 'effect' is used to mean a biological change caused by an exposure. This effect can be measured on a graded scale of severity, although at other times one may only be able to describe a qualitative effect that occurs within some range of exposure levels. When a graded effect takes place a relationship between dose and the gradation of the effect could be established. The dose-effect relationship is the relationship between lead concentration in industrial air and the concentration of ALA in urine samples from workers.

The term 'response' is used to mean the proportion of a population

that demonstrate a specific effect, and its correlation with
estimations of dose provides the dose-response relationship.
Example: a dose-response relationship might compare different lead
concentrations in industrial air with the percent of the exposed
workers that have greater than 5 mg. ALA/l urine.

The term 'dose' is used to define the amount or concentration
of a given chemical at the site where it's presence leads to a given
effect. When the term 'dose' meaning "amount administered to.." is
used it should be specified as "administered dose", "oral dose",
"injected dose" etc.

There are some difficulties in the estimation of dose for lead:
for example, blood concentration is sometimes taken as a measure of
the dose in spite of the absence of adequate knowledge as to the
relationship between the blood concentration and the exposure or the
blood concentration and the concentrations in critical organs.

8.2 Absorption of Lead

8.2.1. Absorption by inhalation

Absorption by inhalation is influenced by three processes in
the lung:

deposition

mucociliary clearance

alveolar clearance

After deposition in the nasopharyngeal tracheobronchial or alveolar
tract, lead may be transported by the intestinal tract or absorbed
into the blood.

The fraction deposited in the nonalveolar compartments of the lung

participates mainly in the first-named type of translocation. The portion deposited in the alveolar compartment is more likely to be absorbed, but may take different routes. Deposition of particles in the alveolar and tracheobronchial - nasopharyngeal compartments of the lung was considered to be dependent on the physical characteristics of the aerosol (such as size, shape and density of the particles and also on the parameters of respiration - nose or mouth breathing tidal volume and respiratory rate).

The size of the particles will determine the fraction which is deposited in the lung. Percentage deposition increases with the particle size from a minimum of 25 per cent for particles approximately 0.5 μ in diameter to a maximum of almost 100 per cent for particles greater than 25 μ. (Hatch and Gross, 1964).

Deposition of inhaled particles will also vary with increased rates of inhalation. Minimum deposition occurs at a respiratory rate of about 15-20/minute. At lower rates, there is an increased probability of particles settling out by gravity and diffusion of particles increases proportionately with the increase of transit time of the dust laden air in and out of the lungs. At increased rates of respiration, coarse particles are deposited in greater quantity because the force of deposition rises with the increase in air velocity (Waldron and Stofen, 1974).

The lead deposited in the alveolar compartment will be cleared from this compartment by (1) transport onto the mucociliary escalator and thence into the gastro-intestinal tract (2) deposition for a long time

in the pulmonary tissues and (3) passage through the pulmonary tissue
into lymph and blood.

8.2.2. Absorption by Ingestion

Absorption of lead compounds after ingestion via food and
beverages is a major source of exposure, but a substantial part of
metals in particle form deposited in the lung may be transferred to
the gastro-intestinal tract by mucociliary clearance. Forty per cent
of inhaled lead of large diameter which is trapped in the upper
respiratory tract may be swallowed (Kehoe, 1960).

In the Toxicology of Metals (Nordberg, 1976), it was concluded
that the gastro-intestinal absorption of lead compounds in adult human
beings is between 5% and 15%. This figure may be greatly altered by
components in the diet, age, and whether the subject ingesting lead is
in fasting state or not. The absorption of lead was shown to be as
high as 50% in fasting human subjects, while in non-fasting subjects
it was 6% to 14% (Wetherill et al, 1974).

It is probable that under normal conditions not more than five
to ten per cent of ingested lead is absorbed from the gut (Kehoe et al,
1964). In exceptional cases figures in excess of this have been
quoted - for example, 40 per cent found by Imamura (1957).

In man the generally accepted quotient of intestinal absorption
is 0.08 in adults although this average figure conceals wide
individual variations (Waldron and Stofen, 1974).

The mechanism whereby lead is transported across the gut mucosa
has not been worked out, but a number of factors are known to influence
lead uptake, in particular the amount of calcium and phosphate in the

diet. Shields and Mitchell (1941) showed that the concentration of
lead in the soft tissues was increased by lowering the amounts of
calcium and phosphate in the diet, either separately or together.
Sobel et al (1938) showed that calcium reduces lead absorption from
the gut by competing for binding sites on mucosal cells, the effect
being an example of competitive inhibition. An active transport
system may be involved however, perhaps governed in part by the influence
of vitamin D; the presence of vitamin D in the diet increased the
concentration of lead in the blood and the femur. Kostial et al (1971)
gave an alternative hypothesis - that the presence of high concentrations
of phosphate in the diet leads to the formation of insoluble lead
phosphate.

8.2.3. Absorption by skin

Lead can enter the body occasionally through the skin, but for
inorganic lead compounds this way of absorption is of no practical
significance. If the inorganic lead salts are suspended on a lipid
medium as in the case of cosmetics and paints it is possible to generate
lead poisoning through absorption by the skin (Cantrarow and Trumper, 1944).

8.3 Transport and Deposition

Certain amounts of lead may be present in the blood and tissues of
normal individuals who have not been exposed to unusual quantities of
lead. Although lead is not an essential constituent of the body, the
average individual in the community continually ingests or inhales small
amounts of lead. The transfer of lead from the external to the internal
environment is poorly understood but considerable body of data concerning
this transport is in blood.

8.3.1. Lead in Blood

Lead in human blood is associated predominantly with the

erythrocytes, some is present in the plasma protein and a small amount
is in a free ionized form. In one study of the distribution of lead in
blood, the conc.entration in erythrocytes was approximately 16 times
greater than the concentration in serum (Dutt et al, 1964). Analytic
data are usually reported as micrograms per 100 ml. of whole blood or
micrograms per 100 g. of whole blood. Obviously, some serious errors
of interpretation can result from comparing whole-blood concentrations
in people with low haematocrit values with those in people with normal
haematrocit values.

The lead in the blood is in the dynamic equilibrium between the
plasma and the red cells, so that lead is given up from the cells as
the plasma concentration falls.

The speed of uptake by the cells is very rapid and shows similar
characteristics both "in vitro" and "in vivo". The validity of "in
vitro" studies is questionable because lead "in vitro" can be removed
by dialysis with EDTA (ethylenediamintetra-acetic acid) for 24 hours,
whereas lead originally in the cells is not affected. This indicates
that lead normally associated with erythrocytes is only slowly
exchangeable with lead in plasma (Clarkson and Kench, 1958).

Watanabe and Yana (1953) reported that the sites of binding to
the red cells are found on the cell membrane which has a particular
affinity for lead. Jung (1947) postulated that lead is probably bound
to the lipids and lip proteins in the cell membrane and Clarkson and
Kench (1958) mentioned that lead is bound to the red cells as a
peptized lead phosphate solution which then aggregates to form a
mosaic on the inner surface of the membrane.

Lead has affinity towards sulphydril (-SH) groups especially di-thiol groups and is one of the most active of the heavy metals in this respect. Passow et al (1961) suggested that in the presence of lead a series of reactions takes place on the membrane i.e. S-S Bridge breaks open to give S - Pb complex, after which S-Pb-S complex is slowly formed. The same study showed that in the plasma lead is bound to the plasma proteins and it may combine with ligands which contain S, N, or O as electron donors; it binds to amino acids although less avidly than the -SH groups. Stover (1959) reported from her experiments that lead rapidly transferred to the extra-vascular space as the plasma level declined and that there is a dynamic equilibrium between red cell and plasma lead on the one hand and extra cellular and intra cellular lead on the other. It is likely to be the ionic fraction of the plasma lead which is transportable to other body compartments. Hursh and Suomela (1968) postulated that release of lead from the red cells may be relatively slow and it may happen on the death of the red cells. Baltrop and Smith (1971) working with red cell hemolysates have shown that haemolglobin has a greater affinity for lead than the erythrocytes stroma or membrane. Continuing their research, in 1975, they reported that the first step could be a combination of lead at the red cell surface with subsequent transfer through the membrane to combine with haemoglobin. Alternatively, there could be binding to the intracellular non-haemoglobin fractions and subsequent redistribution. On the biological half life of lead in erythrocytes, Baltrop showed that in the presence of EDTA in vivo, it is of the order of 120 minutes contrary to 110 hours reported by Castellino and Aloj (1965).

Blood lead concentration may be used to measure current and recent levels of exposure to lead. In healthy adults and children without undue exposure to lead (such as industrial exposure for adults or "pica" for children) blood lead concentrations range between approximately 10-40 μg/100 ml. in whole blood. Goldwater and Hoover (1967), in a study of 801 samples of blood taken from people from all over the world found values ranging between 15-40 μg/100 ml. Manu et al (1969) tested the blood lead in 325 people not exposed industrially to lead and found a mean value of $21.16^{+}6.8$ ug/100ml.

Wexler and Sobel (1935) postulated that clinical symptoms of lead poisoning are related more directly to the quantity of lead in the serum of plasma than to that in the whole blood, particularly since the lead in the cells appears to be comparatively firmly bound and would not be expected to pass into the tissue fluids and to exert it's toxic effects on the tissue cells.

The concentrations of lead in the blood bears no consistent relationship to the appearance or severity of clinical manifestations of lead poisoning which may be absent at high levels of blood level and may be present at low levels.

There are numerous studies regarding industrial exposure to lead and its correlation with blood lead levels. The level of lead in blood does not increase as much with lead absorption as does that of the lead in urine, but fluctuates more widely - Elkins, (1959). The level indicative of absorption considered dangerous has been given varying values by different authors as does the range of the normal values. According to Patty (1949), 70 ug/100ml - 80 ug/100ml are indicative of non-harmful absorption and between 80 ug/100ml - 150 ug/100ml — harmful. However, 50 ug/100ml. of blood are given as indicative of dangerous

absorption by Egli et al (1957).

The diagnosis of lead poisoning must depend on the presence of clinical manifestations of that condition and the demonstration of lead as the etiological agent. In the presence of clinical symptoms the demonstrations of an abnormally high concentration of lead in the blood is of value in establishing this diagnosis, but it must be emphasised that normal blood values may be obtained in cases of active lead intoxication and that the latter may be absent on subjects with high concentrations of lead in blood. Chamberlain and Massey (1972) reported lead poisoning in a patient working as a smelter on a process where lead was used. Extremely high levels of blood lead, up to 1050 ug/100 ml. were found despite only trivial clinical symptoms.

The presence of abnormally large amounts of lead in the blood result either from absorption from the outside, or mobilisation from deposits previously stored in the tissues - (Cantarow and Trumper, 1944). Active mobilisation from the bone, with the development of acute episodes of lead intoxication may occur many months after exposure to lead has ceased. This may occur either spontaneously or as a result of the action of one or more factors which favour the mobilisation of lead such as: the calcium and phosphorous content of the diet and of blood, intake of vitamin D, the stage of skeletal development, the condition of the parathyroid activity and the state of general nutrition with the acid base equilibrium.

On the basis of published work and of experience, particularly in industry, guide lines have been laid down for diagnosis of lead poisoning (Lane et al, 1968). Most people rely largely on the blood lead concentration to make the diagnosis and great weight has been

given to Kehoe's statement that poisoning does not occur if the blood lead is less than 80 ug/100ml. (Kehoe, 1960). Cases of poisoning however have been reported with values of blood lead less than this (Gibson et al,1968; Beattie et al, 1972; Sakurai et al,1974) and conversely patients with extremely high blood lead levels have been found with minimal symptoms (Chamberlain and Massey, 1972; McRoberts, 1973).

The occurrence of low blood lead concentrations in cases of lead poisoning has been discussed by Kehoe (1972); he argues that this apparent anomaly is due to blood being sampled after exposure to lead had ceased, and the concentration falling so that it is below the threshold even though symptoms are still manifested by the patient. This argument is persuasive, but blood lead levels less than 80mg/100ml. have been found in the patients who were still exposed to the source (Beattie et al 1972), and presented symptoms of poisoning.

Vitale et al (1975) criticised the Criteria Document for a Recommended Standard for Occupational Exposure to Inorganic Lead, which regardded lead in blood as the only biological test considered as having practical validity for monitoring the lead exposure of workers. In their work they have shown that a greatly increased body burden of lead as evidenced by EDTA mobilisation tests can coexist with blood lead levels below 80ug/100ml. blood. This is sufficient to cast doubt on the value of the whole blood measurements as a reliable index of the hazard of exposure to and absorption of lead. They quote the blood lead as a test "insufficiently responsive to potentially damaging body burdens of lead to protect workers from occupational lead poisoning". Waldron (1974) suggested that blood lead concentrations should be used to monitor abnormal exposure on a population rather than to serve as a

major diagnostic tool. Used in this way blood lead estimations will
alert the physician or the environmental hygienist to an unrecognised
source of contamination, while at the same time serving as valuable
corroborative evidence of excessive exposures in suspected cases
of lead poisoning. The increasing evidence for subclinical effects is
an indication that every effort should be made to ensure that exposure
to lead is kept to a minimum and that the current threshold values
are too high and need to be set at lower levels. On this basis adult
blood lead concentration should not be permitted to rise above 50 ug/100ml.
and children blood lead concentrations above 30 ug/100ml. Williams
et al (1968) considered lead in blood test to be the best criterion of
absorption. Lane et al (1968) established values for four categories
of blood lead absorption as follows:

Normal	$<$ 40 ug/100ml.
Acceptable	40-80 ug/100ml.
Excessive	80-120 ug/100ml.
Dangerous above	120 ug/100ml.

Normal and acceptable ranges represent the permissible occupational
exposure limits while excessive and dangerous levels are unacceptable
and require appropriate corrective action.

8.3.2. Soft Tissues

Lead diffuses from the plasma into the extravascular space and
then enters the cells of tissues. Lead appears in the cells of the liver
and kidney within an hour after administered by injection and appears to
be particularly strongly bound to mitochondria. Repeated washing
fails to remove all lead from mitochondria and this strong affinity
is of particular relevance when the pathological effects of lead come
to be considered (Castellino and Aloj, 1969). The kinetics of removal

of lead from soft tissues closely resemble those of its removal from the blood. The exchange rates for muscles and skin however are slower than those of other soft tissues (Bolanovska et al, 1967).

Kehoe (1964) states that the average normal adult has about 100-400 mg. of lead in his tissues. According to Cantarow and Trumper (1944), from the pre-school age until very old age, lead maintains an average concentration of approximately 0.2 mg. per 100g. in the liver and 0.1 mg. in the kidney. Table 2 summarises the results of a number of studies of tissue lead levels.

Table 2. The amount of lead in different human tissues

Author	Tissue	Fresh weight mg. per 100gm	Dry weight mg. per 100 gm	Ash mg. per 100gm
Tompsett and Anderson	Kidney	0.072-0.355	0.36-1.77	3.00-17.7
Kehoe et al	"	0.02-0.04	0.10-0.20	1.00- 2.0
Weyrauch & Muller	Brain	0.02-0.03	0.133-0.19	1.33-1.99
Hansmann and Perry	Spleen	2.408	12.403	124.03
Hansmann and Perry	Pancreas	3.396	16.981	169.81
Bagchi	Thyroid	0.04-0.06	0.20-0.30	2.00-3.00
Bagchi	Lung	0.03-0.06	0.15-0.30	1.50-3.00
Bagchi	Uterus	0.005-0.047	0.02-0.23	0.25-2.35
Bagchi	Heart	0.045-0.075	0.22-0.37	2.25-3.75
Bagchi	Muscle	0.014-0.7	0.07-0.35	0.70-3.50
Roche Lynch	Bone Marrow	1.75-5.00		
Hansmann and Perry	Placenta	0.392	1.959	19.59
Thompsett and Anderson	Liver	0.08-0.46	0.42-2.31	4.25-23.10

(from Cantarow and Trumper, 1944)

8.3.3. Skeletal Lead

Of the total body lead 90 per cent or more is stored in the skeleton. Lead has been described by Hammond (1973) as a bone seeker, seeking out areas of active bone formation. Waldron and Stofen (1974) mentioned in their book that bone mineral consists of two calcium phosphate pools which are chemically and physically distinct. The first is a crystalline phase consisting of apatite crystals similar to hydroxy apatite and the second is an amorphous non-crystaline phase composed predominantly of calcium and phosphate. Bone apatite crystals are similar to, but not identical with, hydroxyapatite and the size and shape of crystals varies with bone age and with diet. The calcium which has a definite position in the crystal structure, could be replaced by lead. The crystalline structure of the bone gives a very large interface for reactions to take place which may be as much as 180 m^2/g. and bone may be considered as a dynamic structure although only about 0.65 per cent of bone calcium is exchangeable. Aub et al (1926) demonstrated that pulverized bone took up lead in proportion to the amount of calcium lost suggesting simple ionic exchange.

Hunter (1975) describes lead as flowing in the calcium stream in the body and contended that the two elements shared a common metabolism, and these appeared to be sustained by the fact that the parathormone enhanced the mobilisation of both lead and calcium in man. Black and Farmington (1962) have shown that the biological half-time for the loss of radio-lead from the human skeleton is 670-840 days. There is some ill-defined evidence that under certain circumstances lead may be released more rapidly from the bone. Factors which have been

incriminated include acute or chronic infections, disturbances of acid-base balance, fever, fracture, excessive alcohol intake etc. (Cantarow and Trumper, 1944). Kehoe (1960) postulated that a state of dynamic equilibrium is maintained in the human skeleton and he does not believe in a progressive accumulation of lead in bones. A contrary view is expressed by Horiuchi et al (1962) and Schroeder et al (1961), who stated that the concentration of lead in bone, expressed in terms of ash, increases up to the age of 40 and perhaps beyond.

8.3.4. The Nervous System

There are wide discrepancies in the reports concerning the content of lead in the nervous system. Cantarow and Trumper (1944) reported quantities ranging between 0 and 1.99 mg/100mg.ash of brain tissue. Flury (1934) reported that the presence of lead in the nervous system is influenced by the quantity of lead salts administered, the nature of lead compounds and time elapsing since the detection of lead in the nervous system. Kehoe et al (1935) showed that localisation of lead in the central nervous system is much more pronounced following exposure to volatile organic lead compounds than in cases of inorganic lead compounds.

Schroeder et al (1968) reported mean lead concentrations in the ash of brains from different parts of the world and found values of 10, 13, 10 and 13 p.p.m. for America, Africa, India and Japan respectively. Zaworski and Oyasu (1973) determined by the atomic absorption method the lead concentration in 191 brains of normal people and obtained a mean value of 0.50 ± 0.68 p.p.m. in the wet tissue. O'Tuama et al (1976) studied the distribution of organic

lead in guinea-pig brain and found average values of 0.095 ± 0.016 mg/g. wet weight in control animals and 0.427 ± 0.067 mg/g. wet weight in lead poisoned animals.

Regarding the cerebrospinal fluid in lead poisoning, no consistent relationship to the severity or nature of the clinical manifestations or the concentration of lead in cerebrospinal fluid could be established. Cantarow and Trumper (1944) mentioned the normal figure for lead in cerebrospinal fluid ranging between 0.015 and 0.38 mg. lead/100 cc. but values as high as 0.493 mg lead/100 cc., have been observed in patients and experimental animals with severe lead poisoning.

8.4.1. Excretion by Kidney

Urinary excretion of excessive quantities of lead constitute one of the earliest and surest indices of excessive acute exposure to lead. Kehoe et al (1935) indicated that excretion of lead in the urine proceeds gradually i.e. following administration of lead to rabbits, they found that about three quarters of the quantity given was excreted within thirty days, about one-half during the first week.

Pinto et al (1952) made an estimate of lead clearance utilizing whole blood lead concentration and obtained a mean of 0.284 ($\pm$0.103) units. Since they were using whole blood as opposed to plasma concentration, this figure is likely to be a gross under-estimate of the clearance. Whether the renal tubule takes an active part in lead excretion is open to doubt.

Vostal and Heller (1968) investigated lead excretion in man and dogs and found that at low blood lead levels the lead was eliminated

entirely by glomerular filtration as judged by the ratio of lead to
creatinine clearance. With a sudden increase in blood lead
concentration brought about by an intravenous injection, a change was
observed in the relationship between glomerular filtration rate
and the amount of lead excreted. There was some evidence that the
renal tubule was reabsorbing a constant amount of the filtered lead.
This effect was pH dependent i.e. at low pH the amount of reabsorbed
lead increased, but when the pH was high it decreased or entirely
disappeared. Recently they found that the renal tubule cell transports
lead into the urine, perhaps because of the pressure of lead-binding
ligands in the tubular cell. If intracellular ligands bind lead
diffusing in from extracellular fluid then the concentration gradient
between cell and the extracellular fluid will fall, resulting in the
diffusion of more lead into the cell.

Selander and Cramer (1970) and Oxley (1972) postulated that in
a steady state the urine should reflect the blood lead content. Such
a relationship can be shown when means of blood lead concentration and
urine lead concentration are compared in large groups of adults with
or without undue lead exposure.

How closely does the urinary lead excretion reflect the total lead
body burden? Urine lead levels following kelation have frequently been
cited as a measure of body burden (Zielhuis, 1971). Urinary lead
generally correlates with blood-lead levels but changes even more
rapidly following industrial exposure than does blood-lead.

Barry and Mossman (1970) showed that in a person without undue

entirely by glomerular filtration as judged by the ratio of lead to
creatinine clearance. With a sudden increase in blood lead
concentration brought about by an intravenous injection, a change was
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rapidly following industrial exposure than does blood-lead.

Barry and Mossman (1970) showed that in a person without undue

lead exposure, the daily urine lead excretion represents approximately
0.02% of the total body lead store (based on average daily excretion
of 50 mg. and an average total body burden of 220 mg.). The percentage
is even less in persons with elevated body stores.

It is not surprising then that lead excretion can give a false
impression of the stored body lead, e.g. patients with chronic lead
nephropathy frequently have urinary lead levels within the normal range
despite markedly elevated body stores. Similarly, subjects with heavy
lead exposure in the past can have normal urinary lead excretion despito
large body stores (Baloh, 1974).

Because of the variability of laboratory analysis of blood, Goodman
and Gilman (1965) recommend urine lead level as the best indicator of
severity of exposure. Williams et al (1968) reported that urinary
lead levels reflected blood lead levels fairly well and can thus be
regarded as a useful test of lead absorption. However, it is not so
suitable as blood lead as numerous factors other than degree of lead
absorption alone influence the urinary exfretion of lead, such as renal
function, fluid intake and specific gravity of urine.

Kehoe (1960) and Thompson J. (1971) have found that the normal
urinary lead excretion in adults is approximately 30 ug/litre with a
normal range or approximately 10 ug - 80 ug/litre. Dinischiotu et al
(1960) during their investigations in lead industries found that
sometimes, while the levels of blood lead lay within relatively narrow
limits, the urinary lead values showed large difference, and at times
they found no correlation between the values of blood lead and those of

urinary lead excretion. Lane et al (1968) defined the urinary
lead for the four categories of lead absorption as follows:
normal up to 80 ug/litre, acceptable from 80 to 150 ug/litre,
excessive from 150 to 250 ug/litre, dangerous above 250 ug/litre.

8.4.2. Excretion by gastro-intestinal tract

Lead excreted in the faeces may come theoretically from one
of the two sources, the bile and pancreatic fluid or the intestinal
wall. The gastro intestinal tract has been found to contain lead in
practically all sections including salivary glands and saliva.
Flury (1934) assumed that lead may be excreted in the saliva and the
mouth secretions only in insignificant quantities. Waldron and
Stofen (1974) mentioned that lead passed into the gut lumen bound to
seralbumin which is then proteolised to release lead. Castellino
and Aloj (1965) showed that lead could be eliminated in the bile
following absorption by the gastro-intestinal tract, but there is no
consistent quantitative relationship between lead content of the
liver and the bile.

In judging the amount of lead in faeces it must be taken into
consideration that it consists in part of that which has been
absorbed and re-excreted in the bowel and in part of that which has
just passed through the intestinal tract. Kehoe et al (1933) stated
that a daily faecal excretion greater than 0.6 mg. could be considered
as abnormal.

9. TOXIC EFFECTS

Inorganic lead has several well known toxic effects on blood,

central and peripheral nervous system, kidney, gastro-intestinal tract, respiratory tract, bone and glands. This chapter discusses the toxic effects of lead which concerns the present work i.e. blood and peripheral nerves.

9.1. Haematological system

The haematological effect of lead when expressed clinically is microcitic anaemia which can be attributed to three factors:

    (a)   inhibition in haemoglobin synthesis

    (b)   shortened life span of circulating erythrocytes

    (c)   the stimulation of erythrocytes.

9.1.1 Inhibition of Haemoglobin Synthesis

Haemoglobin is the red pigment of erythrocytes; it is a conjugated protein consisting of an iron containing pigment haem combined with a protein of the histone class called globin. Haem is an iron containing porphyrin known as iron-porphyrin iX.

The porphyrin nucleus consists of four pyrrole rings joined together by four methine ($=CH-$) bridges. The skeleton of the formula of haem is shown in Figure 1: The four pyrrole rings are numbered I, II, III, IV, the carbon atoms of the methine bridges are labelled $\alpha, \beta, \gamma, \delta$, the position to which side chains are attached are numbered 1-8. Side chains 1, 3, 5 and 8 are methyl, 2 and 4 are vinyl, 6 and 7 are propionic acid.

Figure 1 The chemistry of Haeme
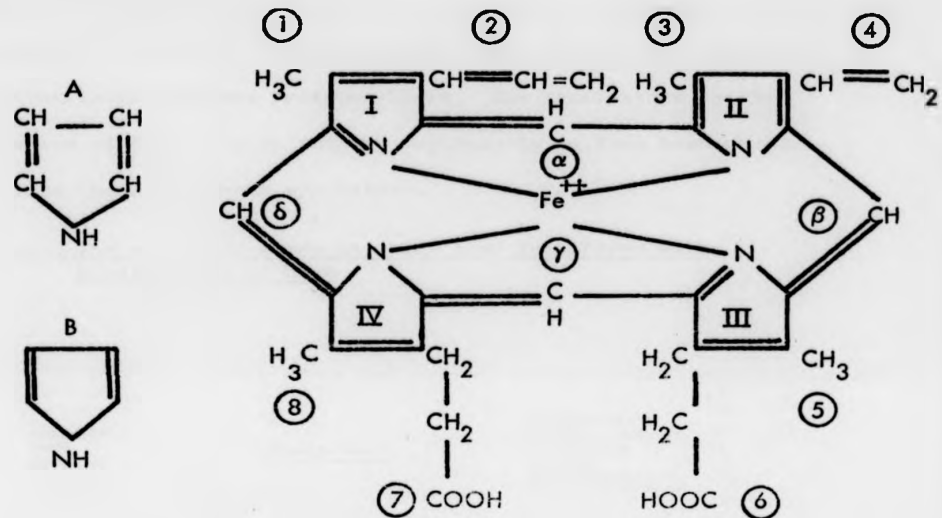
(from Keele C.A., 1965)

The haemoglobin complex when its globin is in the natural
state forms a loose combination with oxygen, the iron being in the
ferrous state. The property which haemoglobin possesses of combining
loosely and reversibly with oxygen depends upon the ferrous atoms of
the haem, each $Fe++$ combines with one molecule of O_2.

Since 1882 when Garrod (mentioned by Cantarrow and Trumper, 1944)
demonstrated porphyrin in urine in a case of lead poisoning, attention
has been focussed on the disturbances caused by lead to haem synthesis.
Lead appears to inhibit the formation of haem at several stages and
these are indicated in figure 2. These stages include the combination
of glycine and succinyl CO-A to form delta amino-levulinic acid (ALA),
a reaction catalysed by the enzyme ALA - synthetase which is the rate-
limiting enzyme of haem biosynthesis. A second stage of inhibition
is the condensation of two molecules of ALA under the enzymatic

influence of enzyme ALA dehydrase to form the monopyrol prescursor

porphobilinogen (PBG). Four molecules of PBG join together to form

a prophyrin, initially uroporphyrinogen III, which by a process of

decarboxilation becomes protoporphyrin. The final stage is the

insertion of ferrous iron into protoporphyrin to form haem which

requires the enzyme haem synthetase.

**Figure 2 The enzimatic steps at which lead interferes with
biosinthesis of haem**
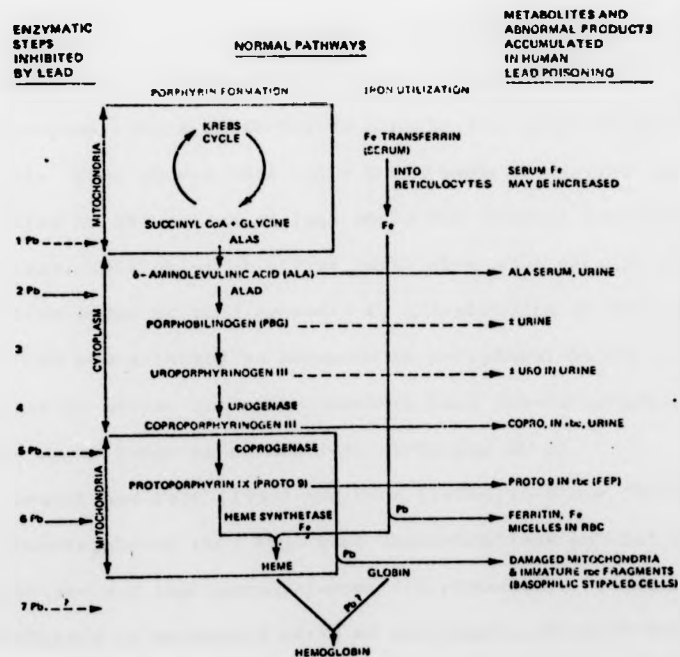
(from 'Lead', National Academy of Sciences, 1972)

Many of these steps in the biosynthetic pathway of haem are
sensitive to the action of very small concentrations of lead, in
particular the enzymic stage of ALA synthetase, ALA dehydrase
and haem synthetase. All these enzymes contain sulphydrill groups
in their active sites (Granic and Mauzeral, 1958). The inhibition
of these enzymes which contain SH groups by the lead is responsible
for an excessive excretion of coproporphyrin and ALA in urine,
an excessive concentration of protoporphyrin in the blood, elevation
of ALA in serum and increase free erythrocyte protoporphyrin IX -
(Goldberg and Beattie, 1972).

The studies on inhibition of haem synthesis by Waldron (1966)
and Goyer et al (1970), were "in vitro" experiments using avian
erythrocytes (these erythrocytes contain the complete haem biosythetic
system). They showed that ALA - D and haem synthetase are the most
sensitive to the action of lead among the enzymes involved in haem
synthesis. Millar et al (1970) postulated that perhaps the most
sensitive index of lead exposure is a depression of the enzyme ALA-D
which can conveniently be measured in peripheral blood. A significant
decrease in enzyme activity occurs at lead levels considered to be
in the upper range of normal i.e. 30-40 ug/100 ml.

Dresel and Falk (1956) and Wada (1976), in other "in vitro"
experiments, showed that high lead concentrations inhibit ALA -
synthestase and coproporphyrinogen decarboxilase. Studies on haem
biosynthesis in erythroid cells of bone marrow from workers exposed
to lead showed a remarkable reduction of the activities of ALA-D and

haem synthetase, a slight elevation of ALA-S activity and a parallel reduction of ^{14}C glycine incorporation into haem and globin. Wada (1976), Bosignore et al (1965), Hernberg and Nikkanen (1970), De Bruin and Hoolboom (1967), and Tola (1973) are few among the many authors who showed depression of ALA-D in circulating erythrocytes and who sustain the opinion of using it as a screening procedure for lead workers.

ALA in urine is another of the tests used in lead absorption. The urinary excretion of ALA is markedly raised in lead poisoning and its appearance in increased amounts is an early sign of metabolic lead poisoning in adults (Haeger-Aronsen, 1960).

According to Lane (1968), ALA in urine in exposed lead workers could be classified as follows:

Normal	$<$ 6mg/litre
Acceptable	6-20mg/litre
Excessive	20-40mg/litre
Dangerous	above 40mg/litre

Raised ALA in urine concentrations are closely correlated with plasma ALA levels, which are elevated prior to the urinary increase (Waldron and Stofen, 1974).

The other tests are for porphobilinogen and uroporphyrinogen. Regarding the excretion of porphobilinogen in urine the position of the authors is still unclear and there has been controversy as to whether urinary excretion is or is not raised in lead workers. De Krester (1963) found that in lead workers porphobilinogen is only moderately raised and in cases of severe poisoning the levels of excretion are inconsiderable.

Increased excretion of porphobilinogen and uroporphyrinogen in human lead poisoning has been reported only in more severly effected cases by Haeger-Aronsen (1960) and Gibson et al (1968). However, these tests are not included among the usual tests for screening in lead poisoning. A usual and valuable test is urine coproporphyrin, mainly izomer III, which is excreted in excess in persons exposed to lead (Montcrieff et al, 1964). This test is used as a screening method for lead workers as it was the earliest biochemical abnormality discovered in lead poisoning (Pinto et al, 1962). According to Lane et al (1968), urine coproporphyrin is included in four lead absorption categories as follows:

Normal	$<$ 150mg/litre
Acceptable	150-500mg/litre
Excessive	500-1500mg/litre
Dangerous above	1500mg/litre

The haemoglobin is another screening test, used much more in old times than in the present. A drop in haemoglobin values accompanied by parallel decrease in the number of red blood cells is usually found in microcytic hypocromic anaemia in lead poisoning. The decrease in Hb precedes the decrease in the number of red blood cells and is more accentuated. However, this parallelism is by no means constant. There have been occasional reports of extreme grades of anaemia in patients with lead poisoning with haemoglobin values as low as 35%, but these were exceptions. In the average case of chronic lead poisoning, the haemoglobin ranges between 75-80% (Cantarow and Trumper, 1944).

There have been numerous studies made of the correlation between blood and urine lead concentrations as tests of absorption, and the use of ALA in urine, PBG, coproporphyrin excretion and haemoglobin concentration as indices of intoxication have been reported (Haeger-Aronsen, 1960; Kehoe, 1960; De Bruin and Hoolboom, 1967; Gibson et al 1968; Waldron 1971). In general a good correlation is found between parameters of intoxication and absorption and in addition the laboratory tests correlate well with lead in air concentration (Williams et al, 1968). The exception is that the haemoglobin levels do not correlate well with other tests (Williams, 1967).

9.1.2. Erythrocyte Life Span

This represents the second cause of microcytic anaemia. In chronic poisoning the shortening of life span is moderate (Rubino et al,1958) but is rarely reduced below 60 days. Using in vivo labelling with tritum labelled dizopropylflourophosphorate it has been possible to show slight shortening (to about 100 days) of the erythrocyte life span in a group of lead workers with blood lead levels between 59 and 162 mg/100ml. blood (Hernberg, 1976).

The mechanism by which lead shortens the erythrocytes life span is not well understood. (Harris and Elsea, 1967). It might be that in microcytic anaemia the change in size and shape of the red blood cells is responsible for the increased vulnerability. Grigs (1964) and Waldron (1966) showed that the osmotic resistance of erythrocytes from patients with lead poisoning is increased together with mechanical fragility, but the biochemical changes related to the last finding are not well known.

Passow et al (1961) and Hasan et al (1967) added lead salts to erythrocytes in vitro and showed loss of potassium and water. This phenomenon may or may not be related to the fact that erythrocytes membrane ATP - ase activity is inhibited by lead and sodium and pottasium ion transport affected. The effect on the membrane is an early response to lead and appears long before clinical symptoms are obvious. There is also an effect on the uptake of 33_p by the cells, which is reduced in man having severe exposure to lead (Westerman and Jensen, 1963).

The membrane ATP-ase levels return to normal when exposure to lead is discontinued or treatment with EDTA has been given (Secchi et al, 1972).

9.1.3. The Stimulation of Erythropoesis

The third result of lead anaemia is the stimulation of erythropoesis which is manifested by reticulocytosis and basophilic stippling of erythrocytes.

The punctate bosophil count enjoyed considerable popularity at one time, particularly as a means of screening lead workers in industry (Lane, 1949; Ghelberg et al, 1966; Barnea et al, 1968), but has now fallen into disuse.

Rubino et al (1958) and Jandl et al (1959) postulated a correlation between the reticulocytes and the capacity of the erythrocytes to take up iron. They reported raised serum iron concentrations with lowered total binding capacity. The uptake of 59_{Fe} by human reticulocytes was almost completely inhibited by the addition of lead but the inhibition was less marked at lower

concentrations. The incorporation of 59_{Fe} into haemoglobin was almost entirely prevented with the consequence that the amount of iron in the red cell membrane was greatly increased. Reticulocytes from bled rabbits incubated with 10_{mM}^{-4} Pb^{2+} showed only a moderate diminution of cellular uptake of 59_{Fe}, but this was a striking increase in the amount of iron in the stromal faction of hydrolysed centrifuged cells, confirming earlier reports of an accumulation of iron in the stroma of immature cells in cases of human lead poisoning. (Bessis, 1965).

Davis (1947) discussed the connection between cells containing iron-stained inclusion bodies and basophilic stippled cells. Janssen et al (1965) reported that in fact these cells, the iron stained inclusion cells, were reticulocytes and by electron microscopy showed that the differing appearance between stipled cells and reticulocytes was largely due to the different manipulations involved in preparing films for examinations.

Beritic and Stahuljak (1963) showed that stippled cells and syderocytes were separate entities, although iron staining inclusion bodies could co-exist in cells together with basophilic staining material.

Henberg (1976) showed that there is no correlation between stippled erythrocytes and intensity of lead poisoning; however, it has some importance in detecting clinical lead poisoning, particularly when the stippled erythrocytes are found from a routine blood film.

9.2.1. Toxic effects on nervous system

Neurological symptoms attributable to lead poisoning had been recognised since antiquity. Both the peripheral and the central nervous system may be affected by this heavy metal.

Peripheral neuropathy has been studied by a large number of authors being a frequently held syndrome among adults exposed to lead as opposed to children who present more often encephalopathy. In the present chapter the literature in histology, neurophysiology, behaviour of animals, human adults and children exposed to lead will be reviewed.

9.2.2. Histological changes in peripheral nerves

The earliest study of histological abnormalities in lead neuropathy was made by Gombouit (1880). He poisoned chronically guinea-pigs and noted both degenerative and regenerative changes in myelin sheath: he described a disintegration of the myelin sheath in segmental nerve beginning at the node of Ranvier, but after a time the removal of the disintegrated sheath took place and short segments of myelin were restored. In contrast to the damage of the myelin sheath the axon was unaffected.

Herter (1895) described extensive changes in the spinal chord of a man with wrist drop, colic and encephalopathy. He estimated that up to one third of the anterior horn cells showed disintegration of the chromophil granules, vacoulisation and pigmentation. Approximately one fibre in four of the lateral popliteal nerve was undergoing Wallerian-type degeneration.

Goadby (1909) reported minute haemmorhages in the peripheral nerves in man with lead poisoning and this could explain other

pathological changes found. The primary lesion has been regarded
to be in the spinal cord (anterior horn cells and lateral columns).
Aub et al (1926) and Reznikoff (1927) questioned the possibility of the
changes ascending on the trunk of the nerves, but no exact information
was available regarding the mechanism whereby the peripheral injury
may produce central lesions.

Legge (1929) reported the most significant changes as being
present in the muscle and peripheral parts of the nerve. Ferraro
and Hernandez (1932) in a study on cats and monkeys poisoned by lead
reported that the brachial plexus and the sciatic nerve of each
monkey presented a certain amount of segmental degeneration of
nerve fibres with swelling and fragmentation of both myelin and axis
cylinders. Numerous fibres were surrounded by a swollen myelin
covering. Flury (1934) reported that peripheral nerves show
degeneration, swelling of the axis cylinders and atrophy of dendrites
in man.

Fullerton (1966) in a study on 31 guinea-pigs with chronic
lead poisoning, found that in a number of animals with normal
conduction velocity many fibres were undergoing segmental demyelination
or remyelination. The survival of only a few normal fibres therefore
appeared to preserve motor conduction velocity. Although Wallerian-
type degeneration in some fibres did not produce any slowing in
conduction velocity interruption of the axon and its severance from
the muscle fibre would cause spontaneous fibrillations. The most common
change seen in the peripheral nerves of these animals was a mixture of

segmental demyelination and axonal degeneration. In 8 animals
segmental demyelination alone was found and in another 5 axonal
degeneration was present in the absence of any demyelination.
The earliest change was the widening of the node of Ranvier.
The process of demyelination, which begins at the node of Ranvier
may stop before it involves the whole outer node and a phase of
remyelination may then supervene with no change in the length of
internode.

Lampert and Schochet (1968) studied by electron microscopy
the sciatic nerves from rats poisoned with Pb carbonate. They
found that the centre and the peripheral areas of the nerve were
generally more severly involved. The axons were widely separated
and reduced in number. There was disintegration of the sheaths
starting with disruption ofthe myelin lamellae adjacent to the nodes
of Ranvier. Some vessels within the affected nerves showed marked
endothelial proliferation. There was proliferation and degeneration
of the Schwann cells. The segment of the myelin sheath related to
the Schwann cell disintegrated, beginning at the node of Ranvier.
The myelin lamellae separated after splitting of major and minor
dense lines. The separated lamellae further disintegrated into
membranous blebs. Proliferated Schwann cells projected beneath
the basement lamina or neurolemma and engulfed disrupted myelin
lamellae. Macrophage penetrating through a gap in the neurolemma
participated in the removal of myelin. New myelin lamellae were
formed by the plasma membrane of Schwann cell processes that wrapped

around denuded axons.   There was evidence indicating that the
proliferated Schwann cells again underwent degeneration, leaving
remnants of basement laminae.   Renewed proliferation of the Schwann
cells growing along these membrane resulted in concentric layers of
flattened cells around axons.   The authors suggested that such
repeated degeneration and proliferation of Schwann cells accounted
for the formation of "onion bulbs" in chronic lead neuropathy.

Schlaepfer (1969), from rats intoxicated with lead acetate,
illustrated prominent changes in the supporting cellular elements of
peripheral nerves, spinal nerve roots and spinal ganglia.   Pathological
alterations of the Schwann cells were manifested by widespread
segmental demyelination in the peripheral and spinal nerve roots.
A selective involvement of the capsular cells in the spinal ganglia
was characterised by a proliferation of these cells and accumulation
of numerous dense bodies within their cytoplasm.   These dense bodies
contained a particulate material which had the electron density of
a heavy metallic substance compatible with Pb in unstained tissue.
These findings suggest the possibility of a direct intervention of
Pb in the metabolism of the capsular cells.   An increase of
neurofilaments and a relative paucity of endoplasmic reticulum was
seen in some associated sensory ganglian cells.   More striking neuronal
alterations occurred in the distal peripheral nerves and in the
posterior nerve roots in the form of Wallerian degeneration.

The author concludes by stating that the co-existence of
segmental demyelination and Wallerian degeneration in the peripheral

nerves of lead neuropathy has been postulated to result from a
common metabolic lesion of the supporting Schwann and capsular cells.

Petkau et al (1974) reported the pathological changes of a
patient who died by amiotrophyc lateral sclerosis generated by
lead poisoning. They found loss of myelin in cortico-spinal tracts
on both sides and this loss was accompanied by swollen perivascular
microglial cells and reactive astrocytes. In the anterior pryamidal
tracts the loss of myelin has a patchy distribution but no loss of
anterior horn cells was found. This was associated with a detectable
amount of lead in the tissue of nerve and muscle evidenced by electron
micro-probe analysis.

Boothby et al (1974) postulated the site of lesion as being in
the peripheral nerves in lead poisoning and rejected the theory of a
myopatic disorder based on experiments in which phospho-creatinine
content decreased in the frog muscle exposed to lead salts.

Beattie et al (1975) reported the pathological changes in two
subjects who died of acute lead poisoning as a result of self-injection
of lead and opium. A muscle biopsy was carried out and the intra-
muscular and cutaneous nerves presented marked myelin breakdown with
some axonal degeneration. The type II muscle fibres (miosin ATP-ase
positive) were unusually narrow and the motor end plates seemed to lack
innervation. Electron microscopy showed large tubular cytoplasmic
inclusion bodies in a few muscular fibres. These findings could sustain
the explanation of a lead myopathy.

The following few studies concern the nervous transmission of the
impulse in lead poisoning. Kostial and Vouk (1957) performed experiments

on superior cervical ganglion of the cat to test whether lead ions
influence ganglionic transmission. The investigations showed that
addition of lead ions to perfusion fluid caused a partial or complete
block of synaptic transmission indicated by failure of nictitating
membrane contraction on preganglionic nerve stimulation. This
failure in transmission was accompanied by a reduced output of
acethylcholine from the superior cervical ganglion. The effects of
lead ions could be reversed by increasing the calcium content of the
perfusion fluid.

Babmindra and Kuzminskaya (1965) in an experimental study on
rabbits intoxicated with lead acetate reported alterations in the
synapses most noticeable after 1-2 months. Although the number of
synapses and nerve cells had not increased, many of the synapses were
argentophilic and their size had increased from 5 to 7 microns.
The synaptic loops were thickened, the fibres degenerated and most of
the synaptic structure had no apparent fibres. After 3 to 6 months the
regeneration started from the injured part of the pre-ganglionic fibres
while the argentophilia of the terminal portions of the synapses was
gradually lost and their size returned again to normal.

Manalis and Cooper (1973) showed from studies on pre-synaptic and
post-synaptic effects of lead at the frog neuro-muscular junction that
lead influences both pre- and post-synaptic events in neuro-muscular
transmission with the pre-synaptic one being most sensitive. Lead
reduced the end-plate potential by a pre-synaptic block and could only
block post-synaptically in condition in which the density of

acethycholine-receptor complexes is much lower than it is during end-
plate potential.

Silbergeld et al (1974) studied the effect of inorganic lead on
neuro-muscular function using rat and mouse phrenic nerve hemidiaphragm
preparations. In vitro lead was found to decrease the force of
contraction and to increase the latency between nerve stimulation and
contraction. These effects were not seen when the muscle was stimulated
directly. Responses of lead treated preparations to acethylcholine and
D-methylcholine were unchanged. In addition, neuro-muscular function
was impaired in mice chronically exposed to lead. These results support
the hypothesis of a pre-junctional site of action of inorganic lead.

After this review on pathological changes at different sites of
peripheral nerves it may be concluded that the lesions most often found
in the peripheral nerves in chronic inorganic lead poisoning are
demyelination (Walleriam type degeneration) and axonal degeneration
with pathological alteration of Schwann cells. The studies reviewed do
not throw any light on metabolic lesions produced by the inorganic lead
in the membrane or Schwann cells. A wide range of species of animals
may need to be exposed to lead and the doses varied from high levels
for long periods to single near-lethal doses with two to three weeks
watch on survivors. Moreover, even in those animals with clear
histological lesions in the peripheral nervous system there are obvious
differences between species like guinea-pig and rabbit which develop
a mild paresis in spite of extensive lesions in peripheral nerves, and
the human situation in which a sudden severe palsy may occur with relatively
slight changes in the peripheral nerves.

Neurotoxic effects found in animals should be taken into account in discussions with the same reliability as other toxic effects found in animal studies and with the same reservations when extrapolating the results to man. The behaviour of animals studied should be correlated to their histological changes.

9.2.3. Neurophysiological changes

The first neurophysiological study mentioned in literature is that of Lane and Levy (1935), who performed chronaximetric studies on lead exposed workers. Chronaxie is a measure of the irritability of conductive tissue in terms of reaction, when electrical stimuli of known intensity are employed. By this procedure prolongation of the reaction time is interpreted as indicative of diminished neuro-muscular irritability. Their studies indicated that lead exposure is accompanied by diminution in nerve muscle irritability, which may never return to normal even after years of freedom from exposure.

Sessa et al (1965) studied motor nerve conduction velocity on 20 patients with chronic occupational lead poisoning. According to their results the reduction in the speed of conduction of ulnar nerve paralleled the increased free erythrocytic protoporphyrin contents. The data showed that the conduction velocities in the lead exposed subjects were reduced as compared with the normal values, although none of the patients showed neurologic disturbances. The authors point out that thd determination of conduction velocities may be useful in the prevention of lead neuropathies.

Fullerton and Harrison (1969) studied nerve conduction velocity

in the lateral popliteal nerve on a group of 19 men who had worked
in a battery factory for 5 to 13 years; all had raised blood lead
levels, some were anaemic, but none had any abnormal neurological
symptoms.   There was no statistical difference between the two groups
for maximal motor conduction velocity nor for the velocity or
amplitude of afferent volley. If slowing of conduction occurred in
only a proportion of the nerve fibres, then maximal motor conduction
velocity might remain normal, but the muscle action potential would
become increasingly dispersed, the longer the conduction distance.
As an indication of dispersion, the amplitude of the muscle response
following stimulation at the knee was exposed as a percentage of that
following stimulation at the ankle. The value for the lead workers
was 84.8% ± 12.7 and for the control group 95.4% ± 6.9. These
differences are statistically significant and suggest that some fibres
in the lead workers were conducting at a reduced velocity.

Catton et al (1970) studied a group of lead accumulator workers
without clinical evidence of neurological lesions. Of the 19 exposed
men, 13 had blood lead levels of 80 ug/100ml. blood. From the
electrophysiological studies, i.e. motor conduction velocity on the
lateral popliteal nerve no difference was found between the exposed
and controls concerning muscle action potential amplitude with
stimulation at the ankle, but with stimulation at the knee there was
a tendency for amplitude to be smaller in the lead exposed workers
than in the controls. Maximal motor conduction velocity was normal
in the exposed group and this could mean that no all of the largest fibres

in the nerves are affected or that the pathological changes are
confined to the smaller fibres.

Hopkins (1970), in an experimental lead poisoning of 15 infant
baboons showed that no abnormality could be found in electromyography
and maximum motor conduction velocity in spite of the very high levels
of blood lead for periods extending up to one year.

Seppalainen (1971) contributed by improving the neurophysiological
methods of detecting sub-clinical lead poisoning. She modified an
old method for testing the conduction velocity of the slow fibres of
the mixed nerves such as ulnar nerve and developed a sensitive method
able to pick up the slowing in these fibres sometimes when motor nerve
conduction was unchanged. In a study on a group of 39 male lead
workers, with chronic exposure to inorganic lead, all without clinical
signs of neurological impairment, Seppalainen and Hernberg (1972)
found that the mean maximum motor conduction velocity of the ulnar and
median nerves were significantly lower in the exposed than in the
controls. The most marked difference between the groups was the
reduction of the conduction velocity of the slow fibres of the ulnar
nerve among lead workers.

Gilioli (1971) reviewed the employment of neurophysiological
methods in early diagnosis of damage of the peripheral nerves fibres
by different toxic substances, among them lead, and recommended the
electromyography and nerve conduction velocity studies as screening
methods for workers exposed to lead.

Vasilescu (1973), in a study on 50 chronically lead exposed workers
with mean blood lead of 72 ug/100ml. blood, measured the electromyography

potentials and the motor conduction velocity of the median, ulnar,
radial and peroneal nerves. Measurement of motor conduction velocity
showed a selectivity of action exerted by lead upon the radial nerve
where a statistically significant slowing was found but only a slight
reduction on the peroneal nerve. The ulnar and the median nerves
were unaffected. The electromiography showed muscle lesions of the
"myositic" type which suggest a direct toxic action of lead upon the
muscle fibres involved.

Mostafa et al (1972) reported electromyographic and motor nerve
conduction velocity studies on a group of 20 lead workers with blood
lead ranging between 21ug-76ug/100ml. blood. The electromyographic
studies were performed on the extension muscles of the forearm, wrist
and fingers and the motor conduction velocities on the radial nerve
and it's posterior inter-osseous branch. In 8 of the 20 exposed they
found evidence of peripheral neuropathy i.e. the conduction velocity
studies showed normal values in the radial nerve but the distal latency
was increased and the evoked motor unit potentials were abnormally
wide. Their conclusion was that the neuropathy they had found was
primary axonal degeneration.

Boothby et al (1974) reported a neurophysiological study on a
worker with chronic lead exposure at an acceptable blood lead. Motor
nerve conduction velocity of the right median nerve and left ulnar
nerve were normal. There was a border-line slowing of sensory
conduction velocity. Electromyography of the right abductor pollicis
brevis demonstrated moderately loss of motor unit and increased

amplitude of the remaining units. Ten months later a slight improvement appeared, the mean action potential duration returned to normal.

Pilat (1975) studied the following group of workers exposed to lead: 42 workers with increased absorption, 88 workers with chronic intoxication without saturnine attacks and 30 workers with saturnine attacks. Of the whole group, 46.9 per cent showed neurophysiologic abnormalities. Changes of electromiographic tracings showed an increase in voltage potential, a large percent of poliphasic potentials and an increase in mean duration of action potentials. The changes were significantly more frequent than the symptoms of anaemia or the functional renal involvements. The electromyographic disturbances persisted for over 5 years after the exposure was suppressed.

Guariglia et al (1975) studied a group of 18 lead exposed workers with a length of exposure ranging from 3 months to 12 years. Motor conduction velocities were significantly decreased for the two nerves studied, i.e. ulnar and peroneal.

Electromyography showed for motor unit action potentials an abnormal number of polyphasic morphologies (>12%). Fibrillation potentials at rest and pathologic modifications of recruitment were found. No relation was shown between electromyographyc findings, exposure time and degree of alterations in plasma and urinary laboratory data. However, it appears that an electromyographic examination is able to reveal a pathology still asymptomatic.

Schlenska et al (1975) reported on two patients with lead poisoning who presented sensory polyneuropathy. They were tested by

electromyography and electroneurogram, both indicated damage to
peripheral nerves which corresponded with findings in an electron-
microscopy study. They also concluded that the early diagnosis of
lead intoxication may be made by electromyographic measurements.

In contrast with the numerous studies on nerve electrophysiology
in adults, there is a rarity of reported cases of peripheral
neuropathy in children with lead intoxication. This could be due to
oversight rather than a true absence of measurable lead toxicity
on their peripheral nerves. The dramatical clinical picture of acute
encepholopathy may overshadow the symptoms of peripheral neuropathy
in children.

Feldman et al (1973), in a study of twenty four Boston children,
with known lead poisoning and blood lead level greater than 40ug/100ml.
blood, reported a reduction in mean nerve conduction velocity of
peroneal nerve as compared with a group of normal children. Landrigan
et al (1976) carried on a study on 202 children with blood lead level
of $\geq$ 40ug/100ml. blood. Among other measurements nerve conduction
velocity in the right peroneal nerve was performed. No frankly
pathologic conduction velocity change was noted.

Although none of the children had any clinical neurologic disease
or frankly pathologic conduction velocities, a close-effect relationship
between conduction velocity and blood lead levels was observed.
These findings are consistent with those found by Seppalainen et al,
(1975)

The conclusion which can be drawn from the present section is
that pathology of lead polyneuropathy is not yet clarified. In

pathological conditions which generates neuropathics (mono or ployneuropathies) such as poisonings with alchohol, vincristine, gold, arsenic, mercury and lead, an axonal degeneration or segmental demyelination appears and this gives a slowing in motor conduction velocity. Conduction velocities are only mildly slowed in axonal degeneration but can be severely reduced to as little as 5 to 10m./sec. in segmental demyelination (McLeod, 1974).

It is of interest to note Gilliat's (1966) point of view, who stressed that "the axon when it is apparently denuded of myelin is still capable of conducting i pulses although at a much reduced velocity" and "during the process of Wallerian degeneration changes in conduction velocity are generally slight". The situation seems to be that if a fibre is capable of conducting impulses at all it does so normally and the most striking change from the electrophysiological point of view is a diminution in the number of functioning fibres rather than a change in conduction velocity. He also showed that if the motor nerve conduction velocity is reduced by 40%, this is likely to indicate the presence of segmental demyelination.

This opinion seems to be in accord with the findings of Fullerton (1969), Catton et al (1970), Mostaffa (1972) and Bootby (1974), who studied people with different levels of lead absorption and did not find the slowing in their motor nerve conduction, but did find other electrophysiological changes in the same nerves.

From the Table 3 (page 58) it can be seen that Fullerton (1969) did not find a low conduction velocity in peroneal nerve, but from

TABLE 3 - Motor conduction velocity in lead exposed people

Source	Nr.subjects	Lead in blood ug/100ml	Nerve tested	MCV exposed m/sec.	MCV controls m/sec.	Results
Catton et al (1970)	19	79-100	Peroneal	49.8 ± 4.7	49.6 ± 3.9	Normal
Vasilescu (1973)	50	27-80	Median	55.6 ± 2.5		Normal
			Ulnar	56.5 ± 2.4		sig.
			Radial	44.8 ± 2.8		sig.
			Peroneal	46.1 ± 1.9		sig.
Boothby et al (1974)	1	> 70	Median			Normal
			Ulnar			Normal
			Radial			Normal
Sessa (1965)	20		Ulnar	35.8-51.6		sig.
			Radial	44.0-60.0		sig.
			Popliteal	38.8-51.6		sig.
Seppalainen et al (1975)	26	20-70	Median	54.5 ± 5.2	58.5 ± 3.8	sig.
			Ulnar	55.0 ± 4.8	58.1 ± 3.1	sig.
			Peroneal	50.6 ± 4.4	52.0 ± 4.0	normal
			Tibial Post	43.4 ± 3.0	44.6 ± 3.2	normal
Mostafa et al (1972)	20	21-76	Radial			normal
Seppalainen et al (1972)	39	40-80	Median	55.3 ± 3.7	58.6 ± 3.7	sig.
			Ulnar	54.0 ± 5.2	56.7 ± 3.4	sig
			Peroneal	48.4 ± 5.1	50.7 ± 3.6	normal
Fullerton & Harrison (1969)	19	> 80	Peroneal			normal
Fullerton (1969)	5	> 80	Peroneal			normal

studying the ratio of amplitude of the EMG response knee/ankle found the value was $84.8\% \pm 12.7$ for exposed and $95.4\% \pm 6.9$ for controls. This difference being statistically significant suggests that some fibres in the lead workers were conducting at a reduced velocity. The findings were similar in her (1969b) work.

Mostaffa (1972) found the conduction velocities normal in the radial and posterior interosseous nerves, (Table 3), but the distal latency was increased in two cases and the evoked M wave was abnormally wide in two cases. Catton (1970) found no difference in nerve conduction velocity - table 3 - or in muscle action potential amplitude with stimulation at the ankle. With stimulation at the knee there was a tendency for the amplitude to be smaller in the lead workers. The value after stimulation at the knee can be expressed as a percentage of that following stimulation at the ankle. For the controls the ratio was $94.5\% \pm 6.4$ and for exposed was $81.5\% \pm 12.5$ ($P < 0.01$) from which it can be seen that there is evidence of an abnormality in peripheral nerve function in some lead workers when the motor nerve conduction velocity is normal.

Boothby et al (1974), table 3, found the motor nerve conduction velocities normal for median, ulnar and radial nerves and a borderline slowing of sensory nerve conduction velocity. Delwaide and Chantraine (1965) studied twelve lead poisoned patients and found that even in the presence of considerable muscle wasting, motor conduction velocity was normal.

In the same table 3, it can be seen that other authors Sessa (1965), Seppalainen et al (1972) and (1975) and Vasilescu (1973) reported from their studies on lead workers significant slowing in motor nerve

conduction velocity in peripheral nerves.

9.2.4. Behavioural Changes

9.2.4.1. Reason for studying behavioural changes

For many years it was widely held that signs and symptoms of lead poisoning would not occur if the blood lead concentration was below 80ug/100ml. blood (Kehoe et al,1935). This concept of a safe threshold value has been subjected to much criticism as it has been shown that mild symptoms of poisoning may occur in occupationally exposed workers with blood lead level above 30ug/100ml. blood and severe symptoms when levels are 40ug/100ml. blood (Bryce Smith and Waldron 1974b).

In children, levels of 40ug/100ml. blood are commonly associated with risk of clinical poisoning but some children appear to be specially sensitive and display serious symptoms even below 20ug/100ml. blood. Since average levels of 30ug/100ml. blood are now reported for groups of children, the problem becomes very serious. What is even more disturbing is the demonstration that behavioural and educational abnormalities can be manifested from children who are not known to have suffered from clinical lead poisoning and whose blood lead level are below the danger level.

Subjective symptoms among lead exposed workers indicative of abnormal behaviour have been reported together with abnormalities of neurophysiological testing and performance. The new problem facing the physician is now that of testing the dynamic function of the nervous system in the intact organism.

Historically, studies on conditioned reflexes and spontaneous

brain activity of animals poisoned with lead has been carried on by
the Eastern European countries researchers, and it will be reviewed
later in this chapter. Researchers from Western European countries
and America have become more and more aware of the new danger of small
levels of lead on work exposed people and on people from the general
environment.

A new field of toxicology, that of behavioural toxicology is now
developing which combines the resources of the toxicologist, the
pharmacologist, the psychologist and the physician which is trying to
determine the deleterious effects of lead on human behaviour, such
as learning, memory, motor performance and neurophysiological changes.
At the present, behavioural toxicology is concerned with:

1) methods for assessing the adequacy of occupational health standards
    and for quantifying and evaluating functional impairment in workers
    based on behavioural performance measures and neurophysiological
    changes.

2) the application of behavioural neurophysiological indications for
    the monitoring and early detection of potential occupational
    health and safety problems.

3) the ultimate establishment of occupational health and safety
    standards based on the preservation of behavioural functions
    and worker capabilities.

9.2.4.2. Behavioural changes in animals

The number of studies concerned with behavioural changes in
animals exposed to inorganic lead are more numerous than similar
studies on human beings. Ungher et al (1957) reported a study on

animals experimentally poisoned with inorganic lead. Two dogs, one well balanced and the other with low balanced nervous behaviour were poisoned chronically with lead acetate. Investigation of the higher nervous activity of the two dogs disclosed cyclic disturbances characterised by prolongation of latency period of response to a positive stimulus. At the end of the experiment an excitation of cerebral cortex appeared, probably as an indication of hyper-solicitation of the nervous cells.

Gusev (1960) reported behavioural impairment when rats and rabbits were exposed to high and low atmospheric concentrations of lead oxide, for six hours daily for six months. Using force and latency-of-response measures, no impairment was seen at an average air concentration of 1.15 ug/m^3 of lead. At the higher concentration 11ug/m^3, disturbed reflexes began to occur about 2 months after the start of exposure and increased in severity over the exposure period. Base-line conditioned reflexes was re-established 10 to 23 days after lead exposure was discontinued. As exposure time increased differential reactions to strong (bell) and weak (light) conditioned stimuli were often disrupted and positive reactions to a negative conditioned stimulus (buzzer) also occurred.

Shalamberidze (1962) using the same methodology as Gusev (1961) found that lead sulphide concentrations of 48.3ug/m^3 (calculated as metallic lead) produced disturbed conditioned reflexes in rates exposed to respirable ore dust. Novakova (1969) using similar conditioning techniques as Gusev (1961), reported that combined chronic doses of arsenic and lead were additive in their effects and disrupted

the acquisition of conditioned reflexes. Their behavioural tests were administered between the fourth and eighth month of chronic poisoning.

Fridland   (1965) reported on three mixed groups of rats and rabbits -

Group I received lead nitrate solution

Group II received mercury bichloride solution

Group III received mercury and lead solution in doses at the level

of the maximal permissible concentrations in the water.

Rats were used for the study of conditioned reflexes, Groups I and II had no deviations in behaviour or conditioned reflexes after a six month period, Group III showed deviation from the normal pointing to neuro-muscular disorders, possibly due to the summation of the two toxic metals.

Xintaras et al (1967) demonstrated that rats given lead acetate (1.5mg/ml in their drinking water) showed altered rapid eye-movement (REM) patterning during sleep. It is interesting that the chronic absorption of lead affects REM sleep and this could be related to the fact that an early sign of lead poisoning is insomnia.

Weir and Hine (1970) have given shock avoidance training to gold fish and then exposed them to specific concentrations of lead nitrate. Tests after 24 and 48 hours yielded significant behavioural impairment at concentrations as low as 0.07 p.p.m.

Carson (1973) reported on a study of the effects of pre-natal lead exposure on post-natal behaviour in sheep. Two groups of ewes fed with lead for 5 weeks before and through gestation, had a mean blood lead content of 5, 19, and 35ug/100ml. blood for the control, low-dosage and high dosage groups respectively. The lambs were not

exposed to lead after birth except for the lead in ewes' milk during the first few weeks of lactation.

The learning ability of the offspring was evaluated in a two choice visual discrimination task when the lambs were 10 and 15 months old; neither the lambs nor the ewes manifested any evidence of lead poisoning; however, learning and visual discrimination was significantly retarded in the lambs from the high dosage group. These findings are particularly important in relation to the public health problem of increased lead exposure in children. Pre-natal accumulation of only 35ug/100ml. blood was sufficient to cause marked retardation in learning.

This is very significant in setting the upper limit of acceptable blood lead content at 30ug/100ml. blood for pregnant women.

Silbergeld et al (1974b) exposed mice to lead from birth, through their mother's milk and at weaning directly through the drinking water. They found a significant behavioural disorder in mice i.e. a significant increase in the level of motor activity. The hyperactivity persisted from birth for at least 150 days. Lead induced hyperactivity was not apparently dose-related and this suggests that increases in motor activity may be an early symptom of low level lead poisoning.

Sobotka et al (1975) reported on effects of "sub-neurotoxic" levels of lead, i.e. levels not producing overt signs of the nervous system involvement. They intubated neonatal rats with lead and noted subtle behavioural changes involving an inability to alternate inappropriate behaviour in a two-way shuttle or a habit-reversal operant task. The

specificity of these central disfunctions was such that motor activity was normal, stress responsiveness remained unaffected and simple learning ability was comparable to that of controls.

The indication for a central neuro-chemical disfunction was that of disfunction of the cholinergic system. These were associated with inhibition of blood ALA-D activity, reduction of brain ALA-D activity, moderate reduction of hematocrit and haemoglobin.

9.2.4.3. Behavioural changes in adults

The present chapter reviews the literature on psychomotor disturbances, subjective disturbances, psychological and peripheral nervous disturbances, visual disturbances and the changes resulted from combined action of smoking and lead, and drinking and lead.

9.2.4.3.1. Psychomotor disturbances

Psychomotor studies have a long history going back to 1890, when researchers included simple motor skill tests in their investigations of "mental" ability (Fleishman, 1953). The tests of motor skills were designed to investigate simple motor abilities and the factors underlying individual differences. Seashore et al (1951) showed that in fine motor skills the sense employed is of moderate significance, the musculature employed is of very slight significance, and the pattern of movement involved is likely to be the most important factor.

In the field of motor ability the subject tested is generally presented with some standardised task in which he must respond by means of certain muscular activities. The term "motor" refers primarily to the muscular activities which can be measured. In this task the subject is responding to some simple or complex stimulus situation, hence the

term "perceptual-motor" or "psychomotor" is often used.

The distinction between perceptual and motor skills is a somewhat arbitrary one, each class of skills being represented in varying degree in the performance of different tasks (Fleishman, 1953). Aptitude testing in the area of psychomotor ability has consisted of individual apparatus tests, where the primary interest is in the motor aspect of the subject responses. Each test consists of a task unit (which the subject operates) and a control unit which consists of the timing apparatus and counters which record the scores and switches which the examiner uses to control the testing period.

The psychomotor tests include such measurements as reaction time to electrical, visual and auditory stimuli, key tapping, two-plate tapping, tremor, finger dexterity, precision and movement aiming. Regarding inorganic lead exposure and psychomotor tests, the literature on this subject is sparse.

Measuring neurological effects of lead in tasks that require rapid psychomotor responses goes back as far as 1954, when Cupcea et al studied 70 lead exposed workers divided into three groups by the length of exposure to lead, and tested for their reaction times to spoken words, visual and electrical stimuli. They found that the latent periods of the motor acts and that of the galvanic reflex were longer in lead exposed people, beginning with their first year of exposure when they do not have any other signs or symptoms of lead poisoning.

Boyadzhiev et al (1962) reported on changes of the latent period and the velocity of locomotor reactions following light and sound stimuli as criterion of early functional changes of the cerebral cortex.

On a group of 136 workers from an accumulator factory, the latent period and the velocity of locomotor function was checked by the chromo reflexograph modified by the authors. The results showed that the latent period was lengthened in men with symptoms of lead poisoning of all degrees and was correlated with age and length of exposure. The authors stressed that the results of these tests may serve as reliable early criteria of lead poisoning and should be evaluated always in parallel with the classic signs of saturnism.

Rubino et al (1965) in a study of early diagnosis of lead poisoning without neurological or electromyographic alterations, applied a new neuro-physiologic method of testing the latent time of the patelar reflex using an apparatus consisting of a stimulation, surface electrodes and an electro-myograph.

Tracings of 18 lead poisoned subjects and 25 controls revealed that the latent time of patelar reflex was significantly increased in 8 cases, none of whom showed alterations of the reflexes or positive signs in electromyography. The average latent time in these cases was 133 m.sec. which is greatly in excess of the normal limit of 114 m.sec. This retardation of the conduction of the nervous impulse is the earliest objective sign of the pathogenic effect of lead.

Milburn (1973) and Milburn et al (1976) reported on three performance tests used in lead exposed workers as tests for subclinical neurological effects of inorganic lead. The three tests were: the two flash fusion threshold, reaction time to a touch stimulus (electrical) and the rate at which hand grip pressure is developed. The three performance tests revealed no differences between the 16 exposed men and

15 controls.

Chaffin et al (1973) presented, for the first time in the field of occupational medecine, a battery of psychomotor tests used in an evaluation of the effects of industrial mercury exposure. Their aim was a major long term objective in developing psychomotor testing methodology for neurotoxic effects, and to use the results themselves as a means of controlling the individual workers' exposure. The tests, later used on lead exposed workers, should be made sufficiently sensitive and selective to detect the first subtle effects of mercury poisoning so that excessively exposed individuals can be identified from the scores, and then removed from exposure before serious effects occur. The tests used in their work were: surface electromiography, forearm tremor, simple reaction time, two-choice decision time, finger and toe tapping speed. They showed that motor functions such as tremor, electromyography, tapping speed were the most affected by increased mercury exposure.

Repko et al (1974) using a similar battery of psychomotor tests as Chafin et al (1973) in studies on lead exposed workers with blood lead levels up to 100ug/100ml., reported on a total of 80 behavioural measures from the performance of 12 different performance tasks.

The strongest relationship between body burden of lead and functional capacity occurred with tests of neuro-muscular function. The specific correlations show that with increases in body burden of lead, functional capacity decreased in terms of tremor and eye-hand co-ordination and increased in terms of muscular grip strength.

In addition, the data suggests that these changes began to occur at blood lead levels as low as 70-79ug/100ml.

9.2.4.3.2. Subjective disturbances

The symptomatology of lead poisoning is protean and may be related to nearly every organ in the body. The purpose of the present paragraph is not a review of the symptoms produced by lead, but of some subjective symptoms possibly connected with our battery of performance tests. Kehoe (1972), in a review of clinical lead poisoning divided the types of clinical symptoms in three categories: alimentary, neuro-muscular and encephalitic, and specified that the last one is very rare in our time, in adults.

No controlled epidemiollogical studies have been found in the literature in which subjective symptoms in lead poisoning were quantatively observed in relation to lead dose.

Sakurai et al (1974) reported on a work about the subjective symptoms in lead exposed workers with levels of lead up to 50ug/100ml. blood. They used a questionnaire designed not only for the examination of lead workers, but also for workers who deal with several other industrial chemicals. Twenty six from the total of 245 questions were allocated to the following lead associated symptoms: constipation, abdominal colic, extensor paralysis, paresthaesia hyperaesthesia, tremor, decrease in grasping power, arthralgia, headache, insomnia, vertigo, loss of appetite, loss of weight, nausea, vomiting, fatigue. When the lead group and the control group were compared as a whole, statistically significant differences were observed in lead symptoms versus total symptoms. There was no dose-

related increase in subjective symptoms up to a blood lead level of about 50ug/100ml.

9.2.4.3.3. Psychological disturbances

Among the psychological disturbances in lead exposed people that of personality and behaviour are more often reported.

Byers and Lord (1943), Goodman and Gilman (1965) reported in their studies such symptoms as irritability and lack of co-operation in groups of lead exposed workers with different levels of exposure; hostility, hyperreactivity and moodiness reported by Byers (1943), hostility, depression and general dysphoria reported by Repko (1976), psycho-neurosis reported by Ambrosi and Secchi (1968).

Fernandez (1967) mentioned saturnine neurasthenia, a neurosis with distinct psychic symptoms such as delirium, psycho-motor agitation, psycho-syndrome to dementia and Korsakoff psychosis with amnesia, suggestibility and fabullation. Korolenko et al (1973) reported among psychic disorders in lead workers cerebral asthenia with signs ranging from headache, vertigo, loss of memory to excessive irritability, emotional liability and for some attacks of alarm and anxiety, fear of noise.

Ursan and Suciu (1965) reported headache, excitation and cerebro-asthenic syndrome, including insomnia, in a group of lead workers exposed chronically to lead. Aub et al (1926) reported alteration in mental attitude, such as general sluggishness and dullness of mentality, restlessness, irritability, insomnia or disturbed sleep with bad dreams, loss of ability to concentrate and vertigo.

Tanquerel (1848) and Hamilton (1929) studied the frequency of
headache and described it as being localised chiefly to the occipital
and temporal regions and occasionally in the frontal regions and vertex,
being dull or throbbing and being accompanied by dizziness, faintness,
emotional and nervous excitement.

Repko et al (1974) reported in their study on behavioural effects
of occupational exposure to lead, that lead exposure up to 100ug/100ml.
blood is related to an increased depression and on the average the
psychological impact of working in a leaded environment is one of
increased hostility, depression and general dysphoria.

All the studies reported had been related to rather heavy and chronic
exposure to inorganic lead. In a low, chronic exposure it is expected to meet
minor disturbances, such as headache, irritability, vertigo, that may have
effect on every day life and working relations. Indeed, it is very
difficult to diagnose lead poisoning based only on those symptoms and
the problem is to develop psychological methods of testing people with
sub-clinical lead exposure, sensitive enough to pick up such small
differences in people's behaviour.

Hanninen (1972) developed a battery of psychological tests which
proved their validity in detecting manifest and latent effect of carbon
disulphide. Subsequently, the diagnostic validity of that battery of
tests has been proved with regard to lead poisoning in a study of 48
lead poisoning cases reported by Parland (1972).

Seppalainen (1974) in her report on behavioural toxicologic methods
for assessing chronic exposures mentioned that psychological measures

are very good in testing the short term exposure and have been useful
in showing effects of low concentrations of toxic substances. However,
if somebody is dealing with chronic exposure and exposure to several
different substances, as happens in industry, there is need for
additional sensitive methods to show changes in the functions of
nervous control systems based on neurophysiological and behavioural
methods.

9.2.4.3.4. Peripheral nervous disturbances

As stated by Kehoe (1972) these disturbances are more frequent
in the industrial lead poisoning of our time than the central nervous
disturbances such as encephalopathy.

The neuro-muscular involvement appears often in chronic exposure
to lead and is translated by sensory disturbances, parasis of extensor
muscles of the arm, leg, foot translated by superficial hypo or
hyperasthaesia, sometimes patches of analgesia over the areas involved
or anesthesia, cramps, pins and needles, pains, increased muscular tone,
weakness, fatigue, increase reflexes in extremities especially in
legs (Prodan and Suciu, 1967).

Paralysis may occur suddenly but often develops gradually; it
varies in severity from slight weakness to total loss of power, i.e.
"wrist drop". Paralysis beginning in one muscle group may remain
localised or may involve eventually the entire body.

Cantarow and Trumper (1944) classified the paralysis in chronic
lead poisoning into four types:

1) Anti-brachial type produces the so-called "wrist drop" in which
   the extensor communi digitorum is first affected. It could be

accompanied by atrophy, twitching and tremor of the affected muscles.

2) Brachial type which affects the deltoid, biceps, brachilis anticus and supinator longus. It occurs particularly in occupations with heavy lifting.

3) Arran-Duchenne paralysis which is an atrophy, weakness or paralysis of thenar and hypothenar eminences, producing the so-called "simian" hand.

4) Peroneal type, involves lateral peroneal muscles, the common extensor of the toes and extensor of the great toe and as a result dorsal flexion of the foot, abduction of the foot and extension of the dorsal phalanges of the toe cannot be accompanied.

Ursan and Suciu (1965) reported the results of a neurological investigation on a group of lead workers and summarised their findings as follows: in chronic lead poisoning the polyneuritic syndrome which was not pronounced, involved mainly the lower limbs; it started usually in the neuro-vegetative form and passed into a somatic and sensory form. No case of paresis of the radial nerve was observed.

On the other hand, Ambrosi et Secchi (1968) reported on a group of workers with chronic lead poisoning who developed neuritis and polineuritis and in whom the bilateral involvement of the radial nerve was the most prominent clinical feature.

Legge (1929) described in chronic lead poisoning disturbances of sensations over the affected areas including numbness, tingling, formication, anaesthesia, analgesia and rarely hyperasthesia.

Livesley and Sissons (1968) reported on a case of chronic lead

intoxication mimicking motor neurone diseas. The symptoms found in
that case were spastic gait, left foot-drop, increase in tone of all
limbs, hyper-reflexia, knee and ankle clonus. Campbell and Williams
(1968) reported on a survey of cases of motor neurone disease and found
that throughout Britain 17% of cases gave a history of known contact
with lead in the past.

Usually motor neurone disease shows itself long after the actual
exposure to lead. They concluded that even the etiologic cause of
motor neurone disease is not known, lead is one of the important
factors to bear in mind for patients with this disease.

9.2.4.3.5. Visual disturbances

Symptoms of the eyes involvement in lead poisoning could be
sometimes the most striking manifestation. Cantarow and Trumper (1944)
reported scotomata for colour and form, colour flashes, visual
hallucinations, narrowing of the visual fields and sometimes blindness
which may come suddenly and be complete in a few hours and may disappear
as rapidly. These symptoms may occur not only with the overt symptoms
of lead poisoning, but also in the absence of other symptoms (Baghdassarian,
1968).

As Lange (1969) and Melnicova (1964) reported, lead could effect
the visual system through the optical nerve resulting in lead optic
neuritis, via the circulatory system as a result of haemmorrhages
in the retina, on intra-ocular tension resulting glaucoma and paralysis
of intrinsic and oculo-motor muscles of the eye. An early sign of lead
poisoning has been described by Sonkin (1963), as a greyish stippling
of the retina.

9.2.4.3.6. Gastro intestinal disturbances

These complaints are probably the most common presenting symptoms in subjects with chronic lead exposure. They also could be the earliest site of obvious disfunction and bodily distress (Kehoe, 1972).

Usually there is a metalic taste which has been attributed to some abnormality of the nervous mechanism for taste perception or to the presence of lead in saliva. There is a loss of appetite, particularly in the morning, which often amounts to a distinct aversion to consumption of food (Sakurai et al, 1974). As Aub et al (1926) showed, early deranged gastric function may be dependent upon abnormality of secretion and motility expressed by diarrhoea which may occur in small proportion of cases; constipation,which is a rule particularly before colic. Nausea or vomiting could appear in 30-40 per cent of cases independent of colic.

In acute plumbism there may be marked salivation with metalic or burning taste in the mouth, acute epigastric pain, hiccough, vomiting and diarrhoea. The character and severity of these manifestations depend upon the irritating properties of the lead compound ingested.

Johnstone (1964) summarised the alimentary symptoms of the inorganic lead poisoning as follows: bad taste in the mouth, tenderness, abdominal pains, constipation and infrequently diarrhoea, anorexia and weight loss.

9.2.4.4. Behavioural changes in children

Byers and Lord (1943) in a study of a group of children supposedly cured of mild lead poisoning found that a high proportion developed permanent neurological and behavioural sequelae. They observed that the children had educational disabilities resembling dyslexia, a tendency

to impulsive and violent behaviour, poor tolerance or frustration and other manifestation of a hyper-activity syndrom.

Perlstein and Attala (1966) studied a group of 425 children with chronic lead poisoning from whom 39% were left with permanent neurological sequelae.

Chisholm and Kaplan (1968), in their review of the consequences to childhood lead poisoning, indicate that the relationship between disfunction of cognitive, behavioural and social performance, and overt encephalopathy is uncertain. Furthermore, these relationships are complicated by the observation that the symptom clusters do not necessarily remain stable. For example, as puberty approaches, some behavioural problems such as aggressivity disappear. Unfortunately, it is also possible that the new problem in behaviour emerge from unspecified developmental process, as it is sometimes seen in children suffering from minimal brain disfunction, a syndrome incidentally compatible with the etiology of lead poisoning.

Antal et al (1968), in a survey in a town where extensive lead working was carried on, found that children were less developed physically and their scholastic abilities were less than a matched series of children from a control town.

The atmospheric lead concentration in the town ranged from $5.2-16.4mg/m^3$ whilst the control town level was $1.1mg/m^3$. None of the children had clinical lead poisoning but it was assumed that the differences seen in growth and development and in intellectual achievement owed their origins to the higher level of lead exposure.

Pueschel (1974) reported on 58 children with an increased body
burden who underwent comprehensive investigations and were re-evaluated
1.5 and 3 years later. Of these children 23-27% were noted to have
minor neurological disfunction and various forms of motor impairment
during each evaluation. While the initial psychological assessment
revealed low average mental abilities in the majority of children,
during follow-up examination a significant increase in certain areas
of intellectual functioning was observed.

Kotok (1972) compared the development of children with elevated
blood lead levels with that of controls. He found deficiency in fine
motor functions and language development in both groups and there was
no significant difference in their performance. The author interpreted
his results as indicating that the observed developmental lag was not
due to lead toxicity but the deficiencies were directly related to
inadequacies in the children's environment.

David (1974) compared a group of hyperactive children with a non-
hyperactive control group on two measures, blood lead levels and post-
penicillamine urine lead levels, which reflect the presence of body
lead. He had concluded that there is an association between
hyperactivity and raised lead levels and that a large body lead burden
may have consequences that have hitherto been unrealised. He suggested
that the definition of what is a toxic level for blood lead needs
re-evaluation and that the physicians should look for raised lead levels
in children with hyper-reactivity.

Lansdown et al (1974) reported on a large group of children under

17 years of age living in a working class area exposed to undue amounts
of lead. The group was examined in an investigation of the relationship
between blood lead levels, general intelligence, reading ability and
rate of behaviour disorder. There was no relationship between blood lead
level and any measure of mental functioning. Lower levels of intelligence
and higher rate of disturbance were found to be more related to social
factors.

Bryce Smith and Waldron (1974a) referring to Landsdown's (1974)
work, criticised the inadequate psychological testing procedure as
responsible for the negative findings. They mentioned the study from El
Paso - Texas on a very big group of children, apparently healthy,
living in the vicinity of a smelter. The children had a blood lead
level of $\geq$40ug/100ml. blood and were found to have diffuse and subtle
impairment of the fine motor, perceptual and visual-perceptual skills.

Beattie et al (1975) reporte. from Glasgow area, where the water
is soft and the plumbum-solvency from water supply pipes increased, i.e.
lead level in water raised. Water-lead levels were measured in the
homes occupied during the first year of life by 77 mentally retarded
children, age 2 to 6 years, and 77 non-retarded matched controls, and
the homes occupied by their mothers during the pregnancy.

The water-lead content was significantly higher in the retarded
group and the probability of retardation was significantly increased
when water levels exceeded 800 ug/litre. Blood lead levels were also
significantly higher in the retarded group.

Landrigan et al (1975) studied forty-six children symptom-free, aged 3 - 15, with blood lead concentrations of 40-68ug/100ml. living within 6.6 km. of a smelter.

Psychological testing and psychomotor tenting, showed age-adjusted performance I.Q. to be significantly decreased in the group with higher lead - levels. Children in all ages in the lead group also had significant slowing in finger-wrist tapping test. Full-scale I.Q., verbal I.Q., behaviour, and hyperactivity ratings did not differ.

Baloh et al (1975) studied twenty-seven asymptomatic children with confirmed increased lead absorption for neurophysiological impairment- quantitative neurological test. There was significantly increased incidence of hyperactive behaviour in subjects with increased lead- levels but there was no significant difference in any of the quantitive test results. Uncontrolled variables, especially lead absorption in infancy and adverse environment pressures otherthan lead still raise questions about the relationship between chronic lead exposure and behaviour or intelligence.

Hebel (1976) reported about the mental capability of children exposed to lead pollution in Birmingham. Eleven-plus examination scores for 851 children living since birth in lead-polluted areas were higher on average than those of 1642 children living in two similar, but unpolluted areas of Birmingham. Moreover, within the polluted area those living closest to the source of pollution did not score lower than those living further away who attended the same schools. The results were not significantly affected by adjustment for social class, birth-rank, and

maternal age distributions. The study may be criticised for lack of information on blood lead levels and for assuming that pollution in the area has not changed in the last two decades.

From the literature reviewed on behavioural changes in animals, human adults and children, it can be concluded that the behavioural disturbances in chronic inorganic lead poisoning are protean but not quantitatively determined.

The point in performing another study in this field is to devise and validate behavioural tests to assess minimal damage to nervous systems by inorganic lead exposure.

The first step, as shown by the reviewed studies, has been done by detecting behavioural changes in such exposure; now should follow the second step in which quantitative appreciation of magnitude of these changes should be made.

Some of these studies have been taken in studying a small group of subjects; some of them are descriptive, dealing only with clinical signs associated with lead absorption; only few have studied the effects of lead on human performance or psychological processes; none of them have studied effects of low level exposure in adults; only one (Repko et al, 1974) have measured large samples of workers and attempted to relate body-burden of lead to behavioural functions of adult workers; none of them have studied the correlations between performance, neurophysiologica and biochemical changes at acceptable levels of lead in blood on adult workers.

9.2.4.5. Smoking and lead

It is very well known that among many undesirable effects produced by smoking on human beings, the absorption of a variable amount of lead is one of them. Tobacco smoke is an airborne source of lead - a single cigarette contains an average value of 1 microgram/lead - Schroeder et al (1961), Horton (1965) or 39 p.p.m. equal 41 ug. lead per cigarette (Cogbill and Hobbs, 1957) or 2.5 ug. lead per cigarette in German brands as reported by Lehnert (1967). Thus a person who smokes twenty cigarettes a day, assuming an absorption in the lungs of 50% could absorb 10ug. lead a day, only from these sources.

The ignited end of the cigarette may reach a temperature level above that of melting point (3.7^{o}C) so that an oxide of metal is formed in the stream of smoke which can be rapidly absorbed into the lung and reach the general circulation - Schröeder, (1961).

A high percentage of lead found in cigarette tobacco remains in the ash while only 5% is transferred to the smoke. Once lead is deposited in the lungs, the amount of absorption into the blood depends on factors such as solubility of the particular form of the lead and on clearance mechanism of the lungs.

Also depth of inhalation, frequency, length of cigarette or cigar, standard of filter and amount of tobacco smoked over the subject's life span are all factors that could influence absorption and therefore any positive correlation between lead accumulation and smoking.

Regarding the tobacco consumption in U.K., this is appreciated by the weight of all tobacco goods sold to the public which have been

53.5 million lbs. in 1870 and increased to 247.7 million lbs. in 1970. It has been estimated that the total smoking population of U.K. is 21.8 million of which 12.7 million are male, over 15 years old. Consumption in pounds weight per head for all tobacco goods was 5.6 lbs. per annum in 1971 (La Ferla, 1976).

For people exposed to lead in their working environment the smoking habit could add to the absorption of lead because usually they touch the end of cigarettes with their hands contaminated with lead dust. There is no report of magnitude of such absorption in people exposed occupationally to lead.

Zielinski (1969) reported on the people exposed occupationally to both lead and trichloro ethylene and who were smokers. They showed that inhaled gaseous lead penetrates directly into the arterial blood without being filtered to the liver and inhalation of the cigarette smoke facilitates the entry of lead to the body through the air passages.

The article is calling attention to the hazard of smoking where there is an occupational exposure to lead and trichloroethylene and the author considers that smokers should never be used on work involving exposure to lead.

Lead levels in smokers from the general environment has been reported by Kehoe (1960), Hofreuter et al (1961), and Lehnert (1967), and their results are somehow contradictory; Kehoe and Lehnert reported no difference between the urinary lead or blood lead levels of smokers and non-smokers, while Hofreuter reported significantly mean blood lead levels concentrations (21ug.   /100ml.) in smokers than in non-smokers (16ug.   ./100ml.)

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McLaughlin and Stopps (1973) studied the smoking habits of over 4000 workers from a company considered to have no occupational lead exposure. The mean urine and blood lead levels were found insignificant between smokers and non-smokers. They have drawn the following conclusions: assuming an average value of 1 ug.lead in the smoke inhaled from one cigarette, the lead exposure from smoking one pack of cigarettes per day is comparable to the daily exposure from atmospheric lead in Cincinnati. Since the lead exposure from cigarette smoke has been shown to have little effect on human urine or blood lead levels it is possible that similar lead exposure from urban air would also have little effect on people.

As could be seen from the above studies on smoking, the results are contradictory. Unfortunately there is no study in inorganic lead exposure and smoking habit reported in literature.

In the present study the hypothesis is that a worker with poor performance from a low-level lead environment exposure and with high level of blood lead, could attribute this to heavy smoking.

9.2.4.6. Alchoholism and lead

Ethyl-alcohol = Ethanol ($C2\ H5\ OH$) is made chiefly by the distillation of fermented carbohydrates and it is the active ingredient of many social beverages such as wine, beers, and spirits. Half a pint of beer or a small glass of spirits can be considered to contain 7 grams of alcohol - Moscovitz, (1974).

Horton (1965) stated that a worker who drinks beer will take 0.1 ug Pb per litre of beer and if he drinks wine from 0.08 to 0.86 ug lead/per litre.

Gounelle et al (1967) reported an ingestion of 0.15-1.20 mg.lead
for every person who drinks 1 litre of wine.

Absorption of alcohol from the gastro-intestinal tract is rapid
and quantitative. It amounts to about 58 per cent in 30 minutes, 88 per
cent in 1 hour and 93 per cent in 90 minutes. A 70 kg. man will raise
his blood alcohol by about 15mg/100ml. with every half pint of beer
or small glass of spirits; after five drinks the blood alcohol should
be below 80mg/100ml. which is the limit set by the law in the U.K.
when driving. It takes about an hour for the blood alcohol to reach
the peak level after which the alcohol is normally burnt up at the rate
of one drink (15mg/100ml.) per hour - Moscovitz, (1974).

The symptoms of acute poisoning are due entirely to narcotic action
on the central nervous system. Chronic alcoholism affects the whole body;
there is a general gastro-intestinal catarrah with chronic gastritis,
malnutrition, emaciation, kidney lesions, possibly cirrhosis of the liver,
peripheral neuritis and psychosis.

In judging the alcohol intoxication, lead poisoning should always
be considered, since at relatively small concentrations lead acts as a
poison on certain enzymatic systems, notably dehydrases which are important
in the intermediate metabolism , and since every alcoholic beverage
contains lead in different amounts - Truhaut et al,(1964).

Cardani and Farina (1972) studied the influence of alcoholic
beverages consumption on lead-induced changes of haeme biosinthesis.
They found a highly significant correlation between alcohol consumption
and changes of porphyrine metabolism in the subjects exposed to risk of
lead poisoning.

The authors suggested the hypothesis that such connection might be due on one hand to a higher introduction of lead through alcoholic beverages, and to a greater carelessness at work by heavy drinkers, and on the other hand to a possible synergistic action between alcohol and lead, whose mechanism cannot be explained in the light of present knowledge.

Nagid and Hilden (1975) reported elevated levels of blood lead in patients with alcoholic liver disease. They investigated the effect of alcohol intake on the activity of erythrocyte amino dehydrataose (ALA-D) and found that patients suffering from liver cirrhosis may accumulate lead at an increased rate and that alcohol intake in these patients may cause a release of lead from the liver to the blood and thereby a depression of ALA-D activity.

Few following authors reported on nervous disturbances in alcoholics due to lead content of beverages th y used.

Morgan and Linn (1971) studied the histories of 5 male patients with four alcoholic neurologic syndromes associated with lead intoxication. They stated that when an alcoholic develops neurologic manifestations such as delirium tremens or muscular weakness it is difficult to differentiate them as due to lead poisoning. Although Pb was not the sole etiologic agent, the severity of the poisoning suggested that it played a significant role. They recommended that in any severe alcoholic poisoning with abdominal colic and anaemia with stippling cells in addition to poor orientation, seizures, progressive encephalopathy or severe muscle weakness, specific therapy for lead chelation (EDTA) should be instituted immediately.

Patterson and Jernigan (1969) reported on lead poisoning from "moonshine" whiskey. The diagnosis of lead poisoning was based on elevated serum lead level (>0.03mg.%) and an elevated 24 hour urinary lead excretion (>120ug.) after ethylene - diamin - tetra acetic acid. From 54 alcoholic patients admitting drinking "moonshine" whiskey, 44% had changes in sensorium and 22% had peripheral neuropathy.

Gounelle et al (1967) studied the lead absorption in heavy wine drinkers. Most of the patients with cirrhosis or just heavy drinkers did show pathologic laboratory results for lead. In addition to the sources of lead present in daily life, the amount introduced into the body through excessive wine consumption ($0.85 - 1.0$ mg/day) can contribute to increased lead absorption which accumulates through the years.

Truhaut et al (1964) reported on possible influence of excessive wine consumption in the etiology of lead poisoning. They had analysed by a polarographic method the Pb content of inexpensive commercial table wines. They found concentrations of lead considered as harmless at a daily consumption of no more than 500 ml. of wine but dangerous for alcoholics who drink up to 5 litres of wine per day, thereby ingesting 1.25 mg. lead per day.

Susceptibility to lead toxicity is influenced by a number of nutritional and metabolic factors, ethanol among them. Mahafey et al (1973) reported an experimental study on rats fed with ethanol and with ethanol plus lead. They concluded that blood lead levels were not affected by ethanol alone; rats given ethanol plus lead had slightly higher blood lead values than rats given lead alone. The studies reviewed

in this section had dealt with alcoholism and lead; it is of interest
in the present work to view the relation between alcoholism and
peripheral nerve disturbance. Alcoholism is a disease which could
begin with disturbances of peripheral nerve conduction velocity and
often this is the only sign of an incipient neuropathy. Ramelli
and Zerbi (1962) reported 26 cases of chronic alcoholism in whom 17
had normal conduction velocities and 9 reduced velocities. The
explanation of normal conduction velocities in this work is that
frequently in the course of chronic polyneuropathy some nerves are
spared and have normal conduction velocity.

Mawdsley and Mayer (1965) compared conduction velocity in normal
people and in 76 patients with chronic alcoholism. They excluded people
who had coincidental diabetes and other diseases which might be
accompanied by neuropathy. They found that in alcoholic patients both
motor and sensory fibres are equally affected in both arms and legs.
They found subnormal velocities in patients without clinical signs of
neuropathy; the changes become more marked and extended proximally as
clinical signs increase in severity. They concluded that nutritional
deficiencies, particularly thiamine lack first cause segmental demyelination
in peripheral nerves and later cause degeneration of fibres.

Walsk and McLeod (1970) performed nerve conduction velocities and
sural nerve biopsies on 11 patients with alcoholic neuropathy and found
significant slowing of motor and sensory conduction. They also showed
a reduction in density of myelinated fibres of all diameters in the nerves;
the predominant pathological changes were of axonal or Wallerian

degeneration. In case of acute neuropathy after heavy drinking, active axonal degeneration was present in the nerves while in chronic neuropathy after long heavy drinking there were regenerating fibres in the nerves and little evidence of active axonal degeneration.

As could be seen from all these studies on alcohol consumption the alcohol consumption could enhance low lead absorption to a status when behavioural and neurophysiological changes could appear. The habit of drinking is studied in the present work: it is expected that workers with low level lead exposure in the working environment but heavy drinkers would perform poorer and present more behavioural changes than their controls.

10. METHODOLOGY

10.1 Introduction

As it was shown in the chapters 5 and 6 the aim of the present study is to determine if any decrement in performance is associated with subclinical inorganic lead poisoning as indicated by reduced nerve conduction velocity and if these decrements are correlated with the changes in nerve conduction velocity or with biochemical changes.

Two factories manufacturing lead batteries were selected in which stratification of labour in the relation to ability and cleanliness of job is very much reduced.

The two factories were named conventionally Nr. 1 and Nr.II according to the order in which they were investigated. The work in the Factory No. I was performed in July-August-September 1976, and in the Factory Nr.II in April-May 1977. Factory Nr.I is situated near

Manchester, and Factory Nr.II near London.

The two factories are considered to provide secure and well-paid employment, and are therefore able to select and retain a high grade labour force. New workers were allocated to a job as vacancies arise and may not change for two years. All workers are paid the same, irrespective of job, and in some of the departments men rotate between the dirtier and cleaner job.

The procedure of testing both population from the two factories was the same. The experimenter did not know to which group the worker called to be tested belonged; in this way a bias factor from the experimenter was excluded.

In each factory two rooms for the testing were allocated. One room contained the equipment for the reaction time, one hole test and tremor test; the other room was used for interviewing the questionnaire and for the adding test.

The tremor test equipment was borrowed from The Royal Naval Environmental Health Unit and used on the Factory Nr.I population only; it was not available for the second factory.

The sequence of tests in both factories was:

1. The Questionnaire (the questions were asked by the experimenter).

2. Monitoring the skin temperature.

3. The Adding test.

4. Grip strength, Endurance and Reaction Time.

5. Tapping Test.

6. One-Hole test.

7. Nerve conduction velocity

8. Monitoring the weight and height.

9. Collecting the blood and urine samples.

In the Factory Nr.I the tremor test was performed separately, two days after testing performance. The time taken for testing the psychomotor performance and the nerve conduction velocity was approximately two and a half hours. The time to perform each test was:

The questionnaire - 10 minutes

Adding test - 5-30 minutes

Grip strength, endurance and reaction time - 30 minutes

Tapping test - 10 minutes

One-hole test - 20 minutes

Nerve conduction - 20 minutes

Monitoring the physical parameters and collecting the blood and urine samples - 20 minutes

The detailed background, description of equipment and procedure follows for each test used.

10.2. Population tested

As can be seen from Table No. 4 from Factory I sixty-seven exposed workers and seventy-nine unexposed workers and from Factory II thirty exposed workers and thirty unexposed workers were tested.

TABLE 4 - The number of population in the present study

Subjects	Factories	Number	Total
Exposed	Factory I	67	
	Factory II	30	97
Controls	Factory I		
	" office staff	49	
	" manual workers	30	
	Factory II	30	109

In Factory Nr.I of the seventy-nine unexposed, forty-nine were drawn from office workers, twelve from maintenance staff and eighteen from a nearby power station.

The groups of exposed and controls in Factory Nr.I were the ones used in a study of nerve conduction velocity by Archibald (1976) a few months before the present work started. As one of the aims of the present project is to determine if the slowed nerve conduction velocities of the exposed workers affect their performance, it was considered most important that the same subjects used in the nerve conduction velocity study should be used for the performance study. At the time of performance testing the workers refused to volunteer for another nerve conduction test, so it was decided to correlate the results of performance of psychomotor tests with the nerve conduction velocity study results of Archibald's. There is a difference concerning the number of workers tested; Archibald's groups were 94 and 94 respectively for exposed and controls, my groups are 67 and 79 respectively for exposed and controls, and this was due to the fact that some of the workers were on holiday at the time of the present study.

The departments from which the exposed people came were: pasting, plate cutting, moulding, forming, assembly and lead recovery. Table 5 shows the distribution of exposed people by departments:

TABLE 5 - Distribution of exposed workers by departments

Department	Factory I		Factory II	
	No. of subjects	%	No. of subjects	%
Pasting	18	26.9	6	20
Plate cutting	11	16.5	4	13.3
Forming	14	20.9	7	23.3
Assembly	8	11.9	13	43.3
Moulding	8	11.9	-	
Lead recovery	8	11.9	-	
TOTAL	67	100.0	30	100.0

The control people came from office workers, maintenance and power station in Factory I and in Factory II from maintenance only.

When the data was to be analysed the groups used were:

(a)   for means, standard deviations, lowest and highest values of age, height, weight, length of employment, blood lead, urinary lead and aminolevulinic acid in urine:

      (i)   Factory I exposed

      (ii) Factory I controls

      (iii) Factory I office controls

      (iv) Factory I manual controls

      (v)   Factory II exposed

      (vi) Factory II controls

      (vii) Factory I + Factory II exposed

      (viii) Factory I + Factory II controls

(b)   For analysing performance by analysis of variance and analysis of covariance:

      (i)   Factory I exposed

      (ii)   Factory I office controls

      (iii) Factory I manual controls

      (iv)   Factory II exposed

      (v)   Factory II controls

(c)   For analysing comparisons between pairs of means using "t" test:

      (i)   Factory I exposed versus Factory I manual controls

      (ii)   Factory I exposed versus Factory I office controls

      (iii) Factory I manual controls versus Factory I office controls

      (iv)   Factory II exposed versus Factory II controls

      (v)   Factory I exposed versus Factory II exposed

      (vi)   Factory I manual controls versus Factory II controls

10.3 Questionnaire

Before commencing the experiment the subjects were asked questions relating to their occupational history, nervous system, smoking and drinking habits; information on the length of exposure to lead, present and previous departments in which they had worked, and the shift they were on at the time of the test.

According to the department in which they worked, the controls from the Factory Nr.I fell into three groups: office workers, maintenance workers and workers from the power station; the last two groups were united in the group named manual workers.

The exposed subjects from both factories work alternately in two shifts and were tested either at the time of Shift I (6 a.m. - 2 p.m.) or Shift II (2 p.m. - 10 p.m.).

Questions regarding the subjective symptoms of nervous system, digestive system and visual organ were selected from the literature on the subjective symptoms reviewed in section 9.2.9.3. of the present work. Tobacco consumption was graded as follows:

Grade I   :   1-14 cigarettes/day or up to 3 ozs. tobacco/week

Grade II :   15-24 cigarettes/day or up to 6 ozs. tobacco/week

Grade III: over 25 cigarettes/day or over 6 ozs. tobacco/week.

Alcohol consumption was graded as follows:

Grade I   :   1-14 pints of beer/week

Grade II :   15-50 pints of beer/week

Grade III: over 50 pints of beer/week

The spirit drinkers were graded as:

Low - 1-3 whiskies a week

Moderate - 4-8 whiskies a week

Heavy - over one bottle whiskey a week

A copy of the questionnaire used in this study is given in Appendix 3.

10.4 Reaction time test

10.4.1. Background

Reaction time is the delay between the occurrence of a stimulus event and the initiation of a response to it, and is determined by the period during which the initial response is being prepared; in other words, it is not the time occupied by the execution of response but the time required to get the overt response started. The response cannot come out of the organism quite as soon as the stimulus goes in. The stimulus starts a process going, but the process remains hidden or "latent" inside the organism until it reaches the muscles and produces an observable effect on the environment.

The sense organ must be aroused to activity, the nerves must conduct to the brain and from the brain to the muscles and the muscles must contract and move some external object.

All these steps in the process take time, the greatest part of the delay being in the brain. Even in the simplest possible reaction the nerve impulses coming in from the sense organ have to accumulate and build up enough excitation to arouse the motor areas of the brain and set up a discharge toward the muscles. When the response has to be adjusted to the stimulus, work is done and time is consumed in registering the exact character of the stimulus and organising the motor response. The reaction time, also called the response latency, includes sense organ time, nerve conduction time, brain time and muscle time.

In a reaction time, experiment of the progress of time is represented by a line extending from left to right we have got the fore-signal (P)

stimulus (S) and response (R) marked on it. A diagram of the whole process will look as follows:

P   S   R

Fore-period   Reaction   After period
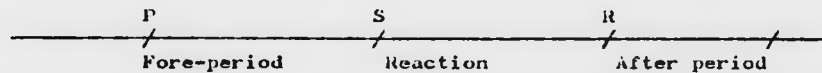
The period P-S equals the fore-period wnich extends from the ready signal or fore-signal (P) to the stimulus (S); the reaction time from S to the response movement (R) and the after period extends from a short to indefinite period beyond R and contains the completion of the motor response.

Reaction time depends on: external factors affecting the organism and internal factors present in the organism in that moment.

Woodworth and Schlosberg (1965) represented schematically the reaction time as:

RT=f(SO) from which RT = reaction time

f = factors

S = stimulus variables

O = internal factors

The S variables are controlled by the experimenter, the O variables are not controllable by the experimenter.

Stimulus factors

Reaction time depends on the nature of the stimulus applied such as: light, sound, touch, etc. Hirch (1861-1864) reported that RT to a visual stimulus is somewhat slower than the auditory or a touch stimulus. Typical values for adult subjects are: 180 m.sec., 140 m.sec., and 140 m.sec., respectively for light, sound and touch.

Regarding the touch stimulus RT differs with the area stimulated, the more sensitive areas are those nearer the brain and these tend to give quicker responses. Sometimes, as Woodworth and Schlosberg (1965) established, an electric. shock applied to the hand or face gives the RT 10-20 m.sec. shorter than the RT to the sound.

Regarding the RT to light stimulus, it differs with the part of retina which receives the light, the farther out from the fovea the longer the RT. Quickness of response goes parallel with acuity of vision; the acuity decreases from the fovea out and the RT increases.

Stimuli such as sight, hearing and touch can be stimulated separately so that we can get a definite answer for any of them; it is complicated with warmth, cold, pain smell or taste, because they cannot be stimulated without incidentally stimulating some touch receptors.

For warmth, cold, pain, smell or taste, the touch receptors receive their mechanical stimuli before the thermal or chemical stimuli can penetrate to them;   the subject gets a touch sensation a fraction of a second before the temperature, smell or taste sensation, so RT obtained are more complicated than that of sight, hearing or touch.

Kiesow (1903) reported values between 308-1082 m.sec. for RT taste, Moldenhaver (1883) reported values 210-390 m.sec. for smell, Woodworth and Schlosberg (1965) reported 300-1600 m.sec. for RT warmth or cold, and Eichler (1930) reported 268-883 m.sec. for RT pain.

As we can see from Table 6 (page 97) RT differs according to the sense stimulated and the differnce might lie in the sense organ, in the nerve conduction velocity, in the sensory nerve fibres which serve these senses or in the nerve centres. Also, the receptor cells may differ in latency or time of reaction.

TABLE 6 - The values of reaction time to different stimuli mentioned by literature

Author	Stimulus	Reaction time values (m.sec.)
Woodworth & Schlosberg (1965)	Light	180
	Sound	140
	Touch	140
Kiesow (1903)	Salt - sodium chloride	308
	Sweet - cane sugar	446
	Sour - citric acid	536
	Bitter - quinine	1082
Moldenhaver (1883)	Noise	164-185
	Touch	187-214
	Odour	210-390
Eichler (1930)	Touch followed by pain	268
	Pain	868
Baxter & Travis (1938)	Rotation - stimulus to semicircular canal	400-500
Chocole (1945)	Sound threshold	400
Froeberg (1907)	Daylight reflected from a square white paper	179-195
Todd (1912)	Light	168-186
	Electric shock	135-152
	Sound	135-160
	Light and shock	139-151
	Light and sound	133-159
	Sound and shock	122-145
	Light, sound and shock	120-138

RT depends on intensity of the stimulus, being long when the
stimulus is very weak and shorter as the stimulus increases to medium
intensities.

In a situation demanding quick response to very weak stimuli,
a small increase in their strength is of great help, but if the stimuli
are already of good strength there is little advantage in making them
stronger - Woodworth, (1965).

The work of Berger (1836) showed that RT is decreasing rapidly
from weak to medium intensities of the stimulus. The curve approaches
a level suggesting that very intense stimuli would not give a much
shorter RT.

Wund (1911) reported that the RT increased again at the high
intensity because, as he explained "one could never be fully ready for
a very intense stimulus", but this statement has never been adequately
tested.

In order to explain why the speed of response varies with the
intensity of the stimulus even when the stimulus is well above the
intensity at which it can be detected, it is necessary to take a dynamic
view of the process of stimulus detection. In a paper on men's sensory
capacity, Fitts and Posner (1967) suggested that the presentation of a
stimulus is always against some background noise, either external or
internal. It is also suggested that a stimulus does not always yield
precisely the same effect within the organism every time it is presented.
In experiments on sensory detection the subject has unlimited time to
make his decision concerning the presence or absence of a signal. He
makes a single decision, and the decision process can be considered a

static one. If the stimulus causes greater activity than some criterion
set by the subject in accordance with the task assigned to him, he
reports a signal, if less, he reports none.

In a reaction time experiment however, speed is stressed and
fluctuations in the information being conducted along the sensory nerve
will affect the rate and accuracy of the decision making process.
Thus the decision making process must be viewed as dynamic in this case,
since it is changing over time.

RT could depend on summation and cessation of the stimuli, a
combination of simultaneous stimuli may give a quicker response than any
one of these stimuli alone. The experiments have shown no great
difference in the RT to onset, or to cessation.

Jenkins (1926) reported quicker reaction to cessation than to
the onset of light. The explanation suggested by him may be in a
better visual fixation of the light that is there, than of the faint
fixation point present before the light is presented.

Woodrow (1915) stated that the nerve centres are in a state of
readiness to respond to either the onset or the cessation of a sound
when it comes simply as a jolt which releases the prepared response.

The internal factors

RT could be dependent on such internal factors as: motivation,
readiness, practice, age, body temperature, alcohol consumption, etc.

Performance is always determined by the level of motivation as well
as by the extent of learning. The term "motivation" is used here in
a broad sense, and it refers to activity level, alertness, fatigue and
other factors besides learning. Example of motivation: in the simple

RT experiment the subject must know in advance what stimulus is coming and what response he is to make. He is motivated by the desire to react as quickly as possible. If the subject will receive the extra motivation - telling him the result of each trial of his performance, or "rewarding" or "punishing" him for his good and bad results respectively - he will speed up considerably.

The quickness of RT could depend on the adequacy of preparation of trial. It will depend partially upon the duration of fore-period; if the fore-period is too short the subject will not have time to get ready, but if it is too long his readiness may fade away. A fore-period of about 2-4 seconds, slightly varied from trial to trial in order to prevent the subject from attempting to synchronize his response with the stimulus, has been generally adopted as about right.

Davis (1940) reported on the muscular tension during the fore-period of a hand reaction. He pointed out that the arm muscles which execute the hand movement become tense during the fore-period.

There are some significant parallels between these fore-period tensions and the properties of preparatory set. The muscle tension begins about 200-400 m.sec. after the READY signal and tend to increase up to the moment of reaction.

The higher the tension at the end of fore-period, the quicker the RT. He concluded that the preliminary muscular tension is the actual response movement in an incipient stage; it is a preparatory activity and it could be regarded as a conditioned response.

Practice is another dependent factor in RT. In the simple RT we expect the subject to reach his maximum speed almost at once or after

a few practice trials. As Woodworth and Schlosberg (1965) showed, the average subject continues to improve for several hundred trials spaced out over several days, although the amount of improvement is certainly not large, after the first 50 or 100 trials. An improvement of about ten per cent after the first day has been noted.

Another factor affecting RT is age. Throughout the developmental period up to 25 years of age the RT decrease, at first rapidly and then more slowly. When the adult level is reached it is maintained without much change up to the age of sixty, after which the RT begins to lengthen slowly. This effect of old age is less marked in RT than in other motor tests - Miles (1942).

Other factors of variability can also be encountered in RT experiments and among them the height-weight index. Smith and Boyarowsky (1945) made a prediction that the men who were heavy for their height gave, on the whole, a slower response than those who were light for their height.

The behaviour of each subject could affect his RT; the skizophrenics had a very long RT, averaging over half a second - Rodnick and Shakow, (1940).

An individual could also vary in his RT from day to day and even from moment to moment. Hull (1942) reported a behavioural oscillation dependent on certain psychological factors such as attention, emotion and sensitivity.

Changes in body temperature connected with the circadian rythm of human beings have been found to have an effect on RT. Kleitman et al (1958) showed that a low body temperature gives a longer RT for auditory

and visual stimuli.

The pulse rate has been studied by Van Biervliet (1894), who reported a quicker RT when the individual pulse rate is high than when it is low.

Consumption of alcohol could also vary the RT. Straub (1938) reported that in an alcoholic with 0.35 per cent alcohol in blood, the simple RT is lengthened by ten per cent and by twenty-four per cent when the alcohol reaches the 1.4 per cent in blood.

Indeed, the number of variables affecting RT could be very numerous and this could explain some intra-individual variation observed in the present study.

10.4.2. Equipment

The setting of the equipment used in the reaction time, grip strength and endurance is shown in Fig. 3.

The equipment used was:

Two cathode ray oscilloscopes (Fig.4)

Physiological stimulator (Fig.5)

Wheatstone bridge (Fig.6)

Hand grip dynamometer (Fig.7)

Differentiator (Fig.5)

Pulse isolation unit (Fig.5)

Sine wave generator for calibration

Pen Recorder

Skin electrodes (Fig.13)

Polaroid camera

A more detailed description of the equipment follows. A Farnell Physiological stimulator with a pulse isolation unit was used to provide

Figure 3 - Scheme of equipment used in testing reaction time, grip strength and endurance
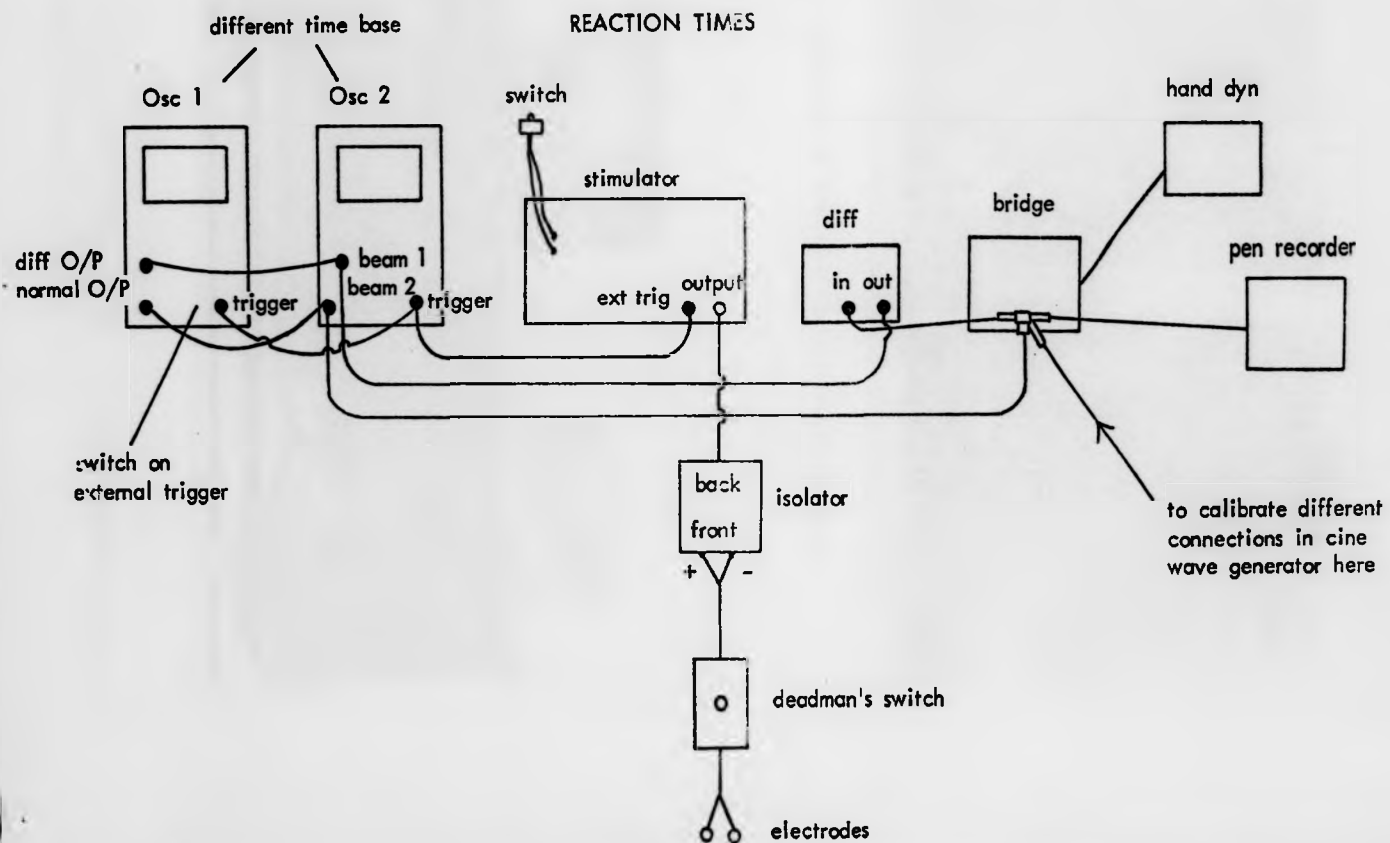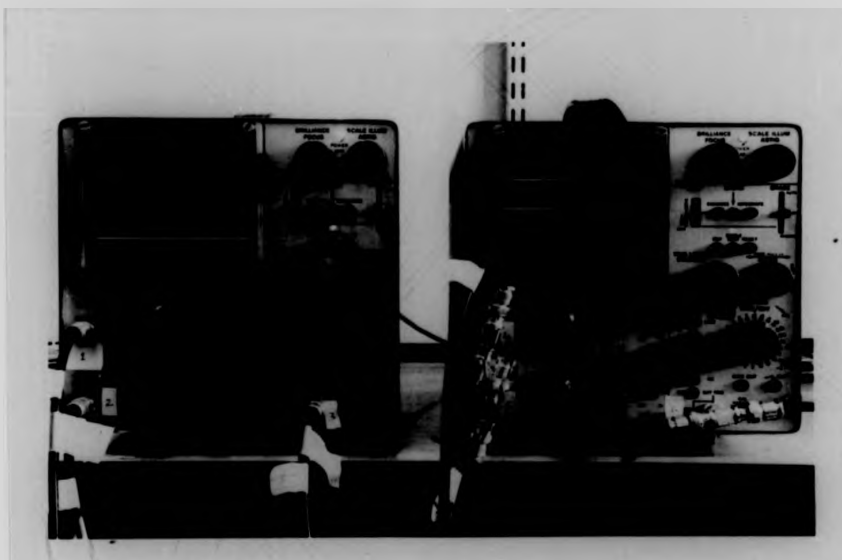
Fig. 4. Photograph of two cathode ray oscilloscopes.
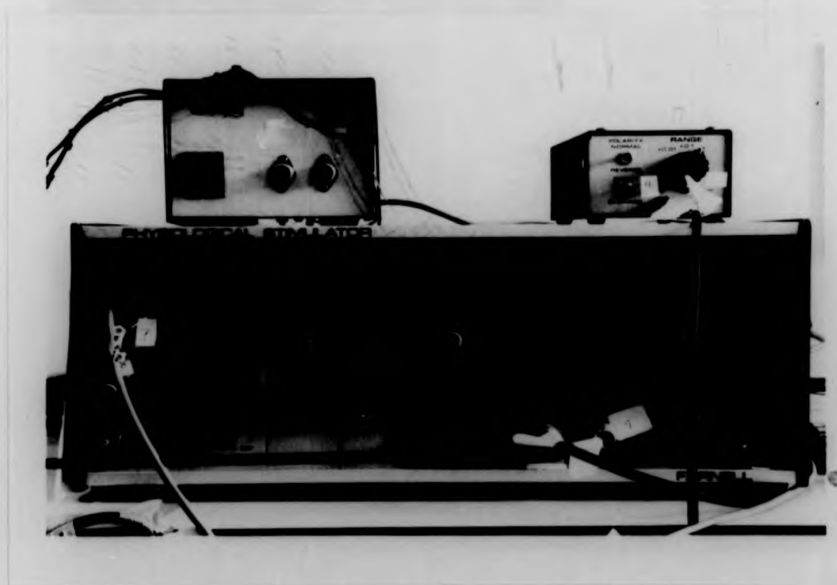
Fig. 5. Photograph of physiological stimulator, differentiator
and pulse isolation unit.
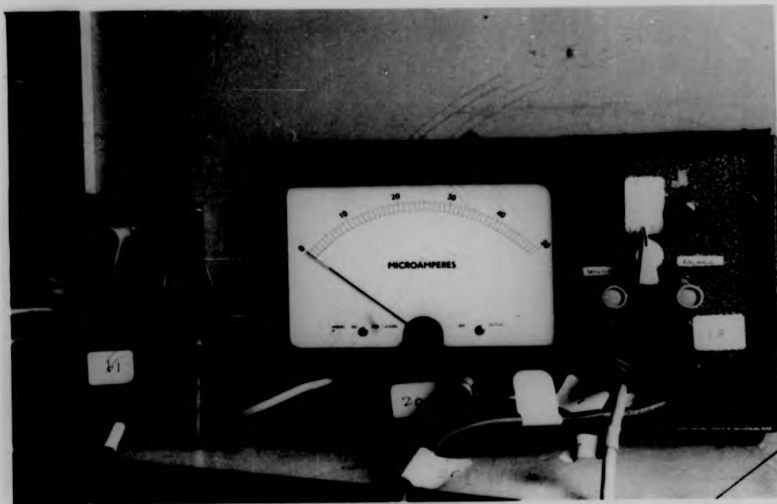
Fig. 6. Photograph of wheatstone bridge.

Fig. 7. Photograph
of hand grip dynamometer.
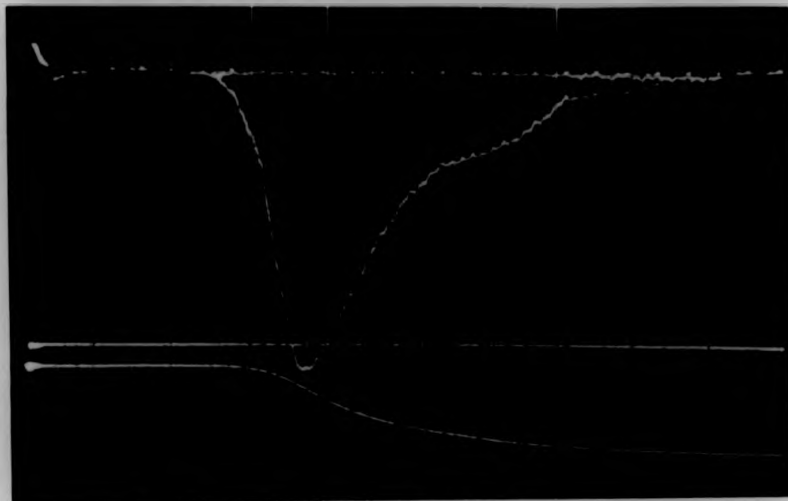
Fig. 9. Photograph showing the oscilloscope trace for arm reaction time.
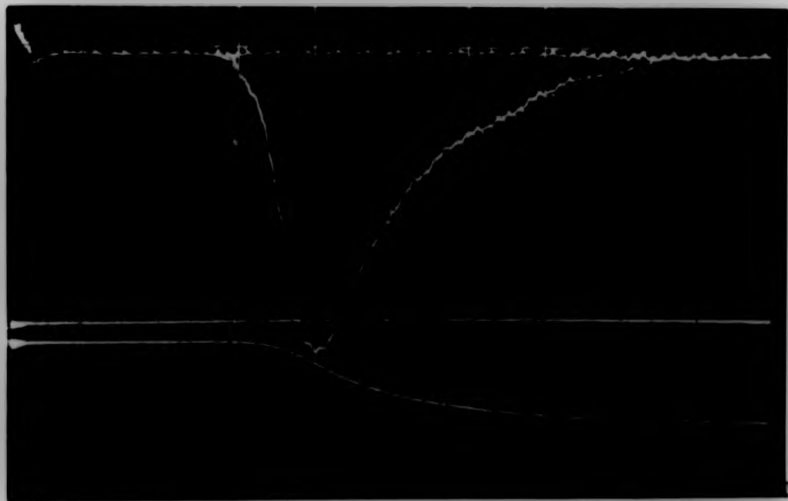
Fig. 10. Photograph showing the oscilloscope trace for leg reaction time.

Fig. 11. Photograph of recorded trace of maximum grip strength
and endurance. (1,2,3, represent the peaks of three
trials for maximum grip strength and the trace between
the two arrows represent the endurance).

Fig. 12. Photograph of subject performing arm reaction - time test.

Fig.13. Photograph of leg electrodes for reaction - time test.

Fig. 14. Photograph of subject performing the tapping test.
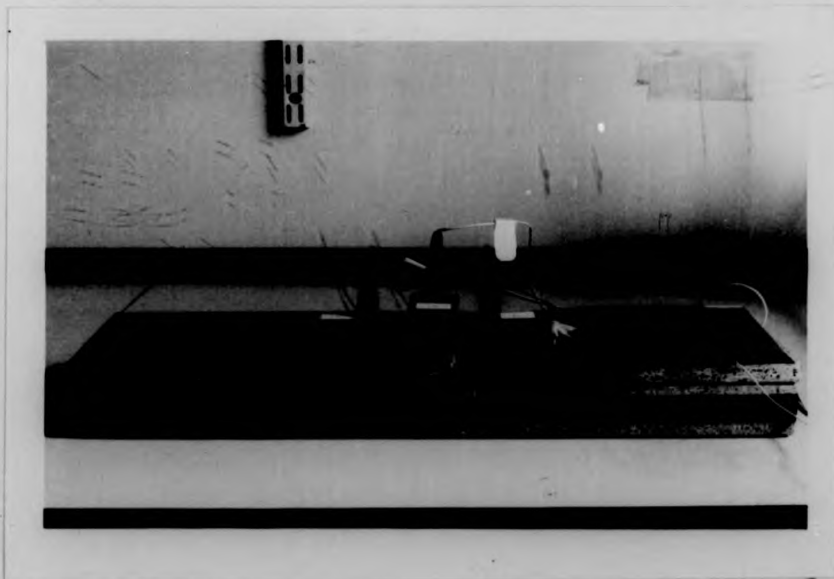
Fig. 15. Photograph of tapping test apparatus.
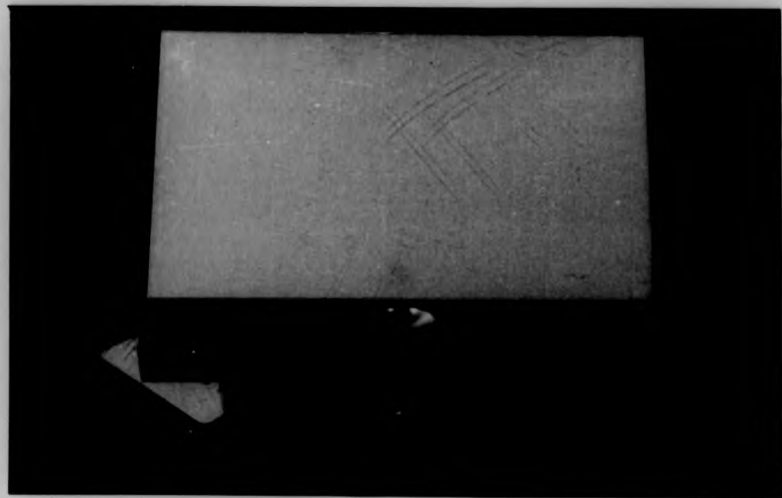
Fig. 17.   Photograph of one-hole apparatus.

Fig. 18.   Photograph of subject performing one-hole test.

Fig. 20. Photograph of subject performing the intention tremor
test.
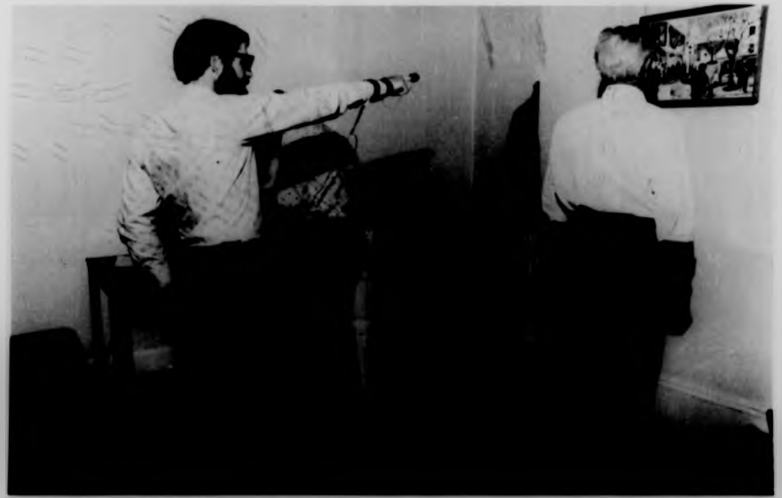
Fig. 21. Photograph of subjects performing the postural tremor
(left) and balance board tremor (right) tests.
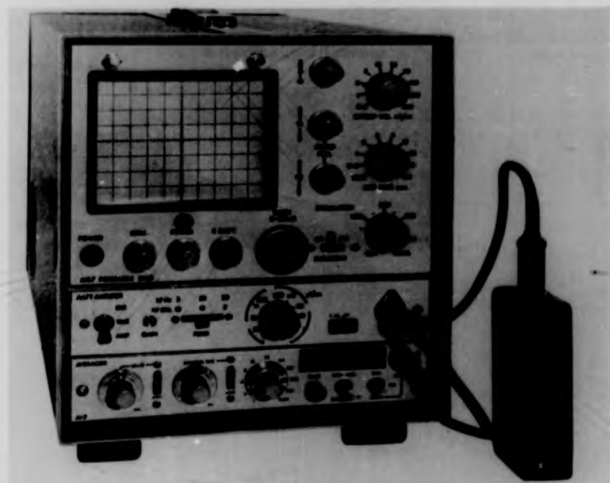
Fig. 25. Photograph of MEDELEC MS 7 electromyograph.

Fig. 26. Photograph of skin thermometer, fibre-optic recorder
and electromyograph.

Fig. 27. Photograph showing the recording electrodes used in nerve conduction velocity tests.

Fig. 28. Photograph showing stimulation of median nerve at the wrist.

the electrical stimuli. This particular apparatus is capable of delivering trains of impulses, single pulses or continuing pulses.

The electrical stimulus used was a single pulse, variable in the voltage in each subject, generally ranging from 40-70 volts. The width of the pulse was 60 ms.

The visual stimulus was a neon flashlight of 20 ms. width confirmed as providing an adequate stimulus in a pilot study, by varying the width of the stimulus and recording the reaction time.

The electrical stimuls was received by the subject via skin electrodes. The stimulating electrodes were of button type, silver discs of 1 cm. diameter mounted on a plastic plate of 6.5/4 cm. allowing for quick reallocation to the skin. The silver electrodes were covered with plastic foam and muslin and when used they were scalded in electrode jelly.

The hand grip dynamometer was used to measure the subject's grip strength, endurance and reaction time to both electrical and visual stimuli.

The dynamometer was of the isometric type with strain gauge forming one arm of a wheatstone bridge circuit, the output of which was connected to a galvanometer for visual monitoring of grip strength and to a pen recorder for recording the grip strength and endurance. The hand grip dynamometer was calibrated by suspending a 20 kg. weight from the strain gauge to a bar; the output of the strain gauge was linear over the range of forces used.

When used for reaction time, the output of the wheatstone bridge was split and fed directly to the oscilloscopes and via a differentiator.

The output of the differentiator was calibrated at 10 hz. using a sine
wave generator so as to give a magnification (gain) of 1:10. The sine
wave generator used for calibration was an RC oscillator type TG 200DM
produced by Levell Electronics, England. The input into the differentiator
at 10 Hz. was 400 mv. peak to peak, and the output 4 volts peak to peak.
The speed with which grip strength is developed can be expressed as
frequency; in calculating the frequency of the hand grip response to
the reaction time stimulus it was assumed that the maximum rate of
change in hand grip occurred at the node of hypotetical sine wave.
The time from the crest to this node i.e. from the start of the reaction
to the point where the maximum rate of change in grip was observed is
equal to 0.25 of wavelength. The frequency in Hz. was therefore
calculated as four times the time between the initiation of the reaction
and the maximum slope i.e. Figure 8:

Figure 8   Diagram of the Oscilloscrope trace
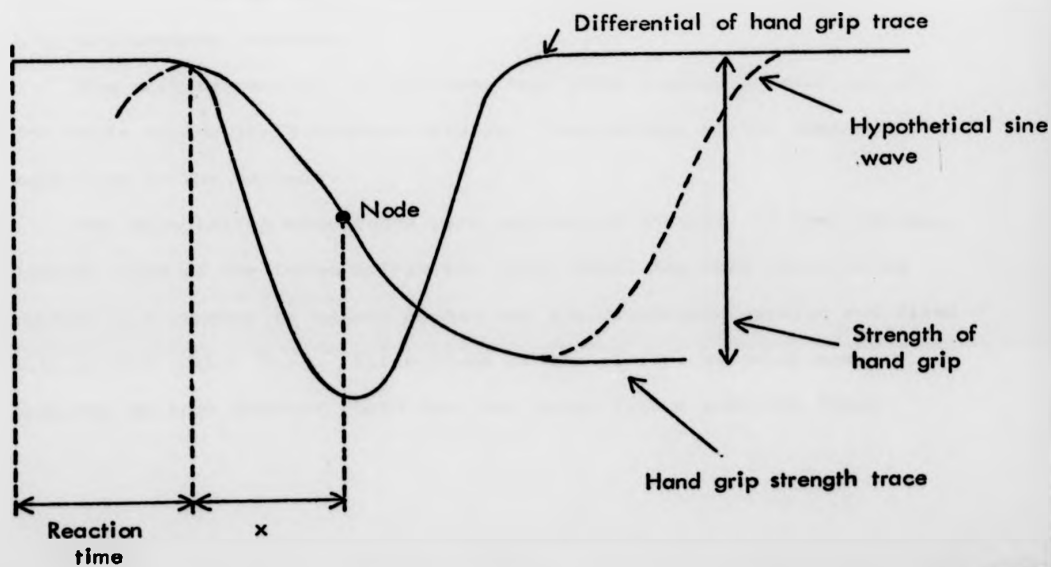
Two conventional cathode ray DM 64 dual trace solid state storage oscilloscopes manufactured by Teleequipment, England, were utilised for display purposes. The oscilloscopes were used to determine the reaction time, the time base being adjusted at 50 m.sec/square on one, the other oscilloscope being adjusted at 20 m.sec/square to give the full response curve and was used to determine the maximum slope and the time to reach the maximum slope. The time base of each oscilloscope was calibrated using a quartz crystal sine-wave generator. The sweep of the oscilloscopes were initiated by a synchronisation pulse from the physiologcal stimulator.

The reaction time to a stimulus - electric or visual - was read directly from the oscilloscopes screens. Also, a record was kept by photographing the trace of the oscilloscopes using a Polaroid CR 9 Lane camera (Figs.9-10) (Page 105).

10.4.3. <u>Procedure</u>

The subjectwas monitored for skin temperature using a skin thermometer - Medizinschen Secundenthermometer produced by Testoterm K G, Fritzschung, Germany.

The skin temperature of the hand was 33-34 degrees Celsius and of the ankle region 31-33 degrees Celsius. The purpose of the test was explained to the subject.

The stimulating electrodes were applied to the skin of the proximal, lateral face of the forearm (Fig.12) (Page 106), the skin first being rubbed with alcohol to remove grease and the electrodes applied and fixed with an ECG rubber band. The voltage of the electrical pulse was adjusted so each subject could feel the pulse like a definite touch

sensation on his arm or leg. The subject was told that the pulse would be presented at irregular intervals, randomly from 2-7 seconds from the time of the command "Ready". The subject was given three practice runs before testing. The reaction time for the electrical stimulus to the arm was the grasping of the hand dynamometer as quick and strong as possible by the subject when feeling the pulse in his arm.

The procedure for the leg was the same as for the forearm, only the electrodes were placed on the lateral face of the leg (Fig.13) (Page 107) five centimeters above the ankle; the voltage required was sometimes higher than that of the arm, ranging from 50-80 volts.

The reaction time to a visual stimulus represented the grasping of the hand dynamometer as soon as the subject saw the flash coming from the physiological stimulator.

The maximum grip strength was calculated as the maximum value in kg. taken from the three trials (Fig. 11) (Page 106).

The endurance represented the time in seconds the subject managed to keep at 75% of his maximum grip strength (Fig.11).

The measurements obtained from reaction time test were:

(i)   Number of volts used as electrical stimulus to arm.

(ii)   Reaction time to arm stimulation (mean of three consecutive trials in milliseconds.

(iii) Maximum slope of curve for stimulation to arm (mean of three consecutive trials) in volts.

(iv)   Frequency of the response for stimulation to arm (mean of three consecutive trials) in Hertz.

(v)   Numer of volts used as electrical stimulus to leg.

(vi)   Reaction time to leg stimulation (mean of three consecutive
       trials) in milliseconds

(vii) Maximum slope of curve for stimulation to leg (mean of
       three consecutive trials) in volts.

(viii) Frequency of the response for stimulation to leg (mean of
       three consecutive trials) in Hertz.

(ix)   Reaction time to a visual stimulus (mean of three consecutive
       trials) in milliseconds.

(x)   Maximum slope of the curve for a visual stimulus (mean of
       three consecutive trials) in volts.

(xi)   Frequency of the response for visual stimulus (mean of three
       consecutive trials) in Hertz.

(xii) Maximum grip strength (kg.)

(xiii) Endurance at 75% value of maximum grip strength (sec.)

10.5. The tapping test

10.5.1. Background

     The tapping test - one plate and two plates - were selected
for the present psycho-motor test battery because tapping abilities
have been tested by other authors when investigating the performance
of workers exposed to mercury, methylene-chloride, carbon monoxide etc.

     The scores of the results reported by other authors - Chaffin
and Miller (1974), Winneke (1974) - cannot be compared directly with the
present work because the test they used differs slightly in detail from
the test used in this study, both in the construction of the equipment
and in the method of tapping, i.e. using a finger without a stylus or
tapping with a stylus in trials differing in length from those used
in this study.

Tapping ability is the speed with which the subject can oscillate either his fingers or his arm. The aim to perform this test is to measure the proximal arm muscle function and wrist flexor and extensor function. The tapping may be regarded as a natural frequency of a neural feedback system as in the following scheme by Sollberger (1965):

Regulation of frequency

Central nervous system

Effectors   Sensors

musculature   touch, muscular, ear,
                                             tension, eyes
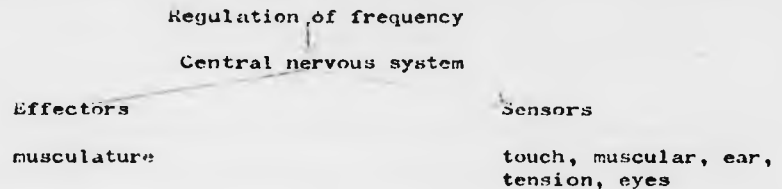
The tapping seems relatively independent of an eye-hand co-ordination ability. Greene (1943) found that when the eye-hand co-ordination is involved in the tasks, the loading becomes smaller on the tapping.

Tapping with the pencil making no effort to tap a particular spot yielded a high loading on tapping.

Tapping in large circles yielded equal moderate loading on tapping.

Aiming and tapping in small circles was difficult and yielded no loading on tapping but high loading on aiming.

The tapping using wrist action, as in the present test, has been found by Melton (1947) to have a large loading on tapping.

Fleishman (1954) in an investigation and definition of psychomotor skills, selected a number of psychomotor tests, among them the two plate tapping, aiming at testing a limited number of abilities which could be useful in describing the performance in a wide variety of psychomotor tasks.

The test used by him was the two plates united by a bridge and the subject was asked to strike them with a stylus as rapidly as possible;

he strikes the plates successively - first one, then the other, making as many taps as possible on the plates in the time allowed. The number of taps were recorded on a counter. The number of trials were six, each of thirty seconds. The author found the two plate tapping as a factor rate of arm movement with a loading of 0.54 in comparison with other arm movement factors such as: Ten Target Aiming - 0.66 and Rotary Aiming - 0.46.

Winneke (1974) used one and two plates tapping test in four trials of 15 seconds each, and in four trials of 20 seconds each, for one and two plates respectively, on subjects exposed to methylene chloride and carbon monoxide.

His results showed a definite impairment of the exposed subjects to methylene chloride but for subjects exposed to 50 p.p.m. of carbon monoxide (low level of exposure) the results indicated better performance for exposed than for controls, an unexpected result which the author could not explain without further research.

Chaffin and Tiller (1974) had used the finger tapping, the toe tapping (left foot, right foot and alternately) in a battery of psychomotor tests in a behavioural and neurological evaluation of workers exposed to inorganic mercury.

Their results showed that the tapping test was one of the most significantly correlated with increased mercury body burdens.

Rates for finger tapping, right foot tapping, left foot tapping and alternate foot tapping were all significantly decreased in those people having elevated mercury burdens.

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Their results showed that the tapping test was one of the most significantly correlated with increased mercury body burdens.

Rates for finger tapping, right foot tapping, left foot tapping and alternate foot tapping were all significantly decreased in those people having elevated mercury burdens.

When the workers having initially high mercury levels were removed from exposure, their mean urine mercury levels decreased and their tapping rates increased on average about 40 per cent, showing a considerable reveral effect.

Regarding the lead exposed populations, studies on tapping had been carried out on children.

Landrigan et al (1975) in a work on neurophysiological disfunction in children with chronic low level lead absorption, included among other motor function tests, the tapping test with a stylus, first on one and then on two plates. The trials given were one of ten seconds for non-dominant hand, and one of ten seconds for dominant hand for one and two plates.

They showed that children in the lead group were significantly slower in finger wrist tapping.

Contrarily, Baloh (1975) using the same methodology as Landrigan et al (1975) and the same equipment, could not find a significant difference between the performance of tapping in a group of children with chronic increased lead absorption and in their controls. The results showed a trend toward poorer scores in tests requiring fine motor abilities i.e. tapping in the elevated lead level group, but there was no significant difference.

10.5.2. Equipment

The tapping equipment used for this work is shown in Fig. 15 (Page 108). The two metallic plates are equal, of rectangular shape, the dimensions being: 14.5/20 cm. The two plates are separated by a bridge 3 cm. wide

and 2 cm. high. The stylus connected to the plates is 15 cm. long
and 7 mm. outside diameter. The two plates are connected to a counter
timed for 10, 40 and 60 seconds, as can be seen in Fig.14 (Page 108).
The counter recorded the number of left plate taps, right plate taps,
number of latches and the number of bridge hits. The two plates plus
stylus were enclosed in an acoustic booth to reduce the noise made when
performing the test which would have disturbed other subjects who
performed simultaneously on other tests in the same room.

The number of taps performed in the single tapping test had also
been registered on a tape recorder and analysed on a level recorder by
counting the impact peaks. It was considered that this gave a
permanent recording of the test so that the results could be checked
and to minimise the recording error.

A stop watch was used to monitor the time of rest between the trials.

10.5.3. Procedure

The subject is seated comfortable at a table which has the
acoustic booth with the test in. The experimenter explained to the
subject the purpose of the test and the procedure. This was followed
by reading aloud the main points of the test procedure from a card
placed in front of the subject.

The test consisted of three trials of one plate tapping and three
trials of the two plate tapping; the duration of the three trials were
10, 40 and 60 seconds respectively. There was a 30 second rest between
trials and 30 seconds rest between single and double tapping trials.

The subject was instructed to start tapping with dominant hand
at the command "go" and to stop at the command "stop". He was instructed

to tap as quickly as possible, keeping his right arm up, not rested
on the table when performing, keeping the stylus in a vertical
position, avoiding hitting the bridge when alternately tapping,
aiming at complete latches. (Fig.14) (Page 108). During the resting
periods the subject rested his arm on the table.

The measurements made for the tapping abilities were:

(1)   Tapping double plates, 10 sec. trial, number of left plate taps

(2)   "   right   "

(3)   "   latches

(4)   "   bridge hits

(5) Tapping double plates, 40 sec. trial, number of left plate taps

(6)   "   right   "

(7)   "   latches

(8)   "   bridge hits

(9)   Tapping double plates, 60 sec. trial, number of left plate taps

(10)   "   right   "

(11)   "   latches

(12)   "   bridge hits

(13) Tapping single plate, 10 sec. trial, number of taps

(14)   "   40 sec.   "

(15)   "   60 sec.   "

10.6. One - hole test

10.6.1. Background

The One-Hole test was included in the present battery of psycho-
motor tests as a measure of steadiness and eye-hand co-ordination.

This test is available from Lafayette Instruments Co. and has been

designed and validated by Salvendi and Seymour (1972); it represents
a modified Purdue and O'Connor test, usually used to measure steadiness
and speed of skill acquisition.

The One-Hole test was developed as a result of earlier
experimentation (Seymour 1959, 1966,& Salvendi 1968) on the acquisition
of industrial skills from which the hypothesis was formulated that the
rate of improvement in the elements of dexterity tests would provide
better prediction of a subject's performance than the gross scores
traditionally used.

Salvendi and Seymour saw neither the Purdue Pegboard nor the O'Connor
finger dexterity test as being sufficiently controlled to constitute
an adequate test of speed skill acquisition, because of the variability
inherent in grasping the pins from the tray, due to the different
distances travelled between grasping and positioning the pin.

In the One-Hole test, the task consists of grasping a pre-positioned
pin identical with that used in the Purdue Pegboard test, moving the
pin to, and placing it in, a hole.

Elemental times (reach, grasp, positioning) rather than the number
of pins inserted per unit of time are important because they do not
improve equally. Due to practice, some improve more than others and
those elements with the highest perceptual load and the greatest
variability in performance time improve the most.

Ward (1974) in an investigation into the effects of hard physical
work on fine manipulative task had used the One-Hole test as measuring
not only the acquisition of fine manipulative skills, but as an indirect

measure of tremor i.e. as tremor levels increase the subjects should experience more difficulty in quickly and accurately picking up the pins and placing them in the hole.

The results of her work indicate that hard physical work increases the time it takes an individual to complete the Pegboard task. Hard work with only the arms causes an impairment of an individual's ability to complete successfully a fine manipulative task immediately on cessation of the work; the effect continues up to 30 minutes. Also, hard physical work with the arms increases the amount of hand tremor experienced by an individual, (the consequence being an impairment in performance of a fine manipulative task.) Even though the four elements of reaching, grasping, moving and placing the pins were not studied individually and objectively in the One-Hole test used by Ward (1974), it was considered from subjective reports and observations that the element of placing the pin in the hole was the most disturbed by errors of overshooting and corrective action of the movement associated with an increased amplitude of hand tremor.

10.6.2. Equipment

The One-Hole test used in this work consists of a time recording counter, and the one-hole test apparatus (Figs.17 & 18) (Page 109).

The time recording counter is connected to the test apparatus and is used to count the time of grasp and positioning in each one minute trial.

The One-Hole apparatus with a built in counter is used for performing the trials and to count the number of pins inserted in the first half-minute of each trial and the total for each trial (Fig.17)

The mechanism of the One-Hole test is dependent on the force of gravity. The pins used are those adopted in the original Purdue-Pegboard

i.e. $\frac{1}{8}$" x 1" in size.

The plastic tube (which connects the grasp and positioning location) is filled with eight pins, one of which is located in the grasp tray. When a pin (at the grasp location) is picked up from the tray the next pins (in the plastic tube) is pushed down into the tray by the gravitational force acting on the other seven pins.

All the pins used in the One-Hole test were cleaned at intervals with alcohol and tissue paper to keep them free of grease.

10.6.3. Procedure

The One-Hole test is administered for seven one-minute trials, with a 5-10 second rest between the trials, in which the experimenter recorded the scores from the counter (grasp and positioning time) and the scores from the built-in counter of the one-hole apparatus i.e. the number of pins inserted in 60 seconds trials. The number of pins inserted in the first half-minute of each trial are also recorded using a stop-watch switched on at the beginning of each trial simultaneously with the switch of the time counter.

The subject is seated comfortably at a table on which the test equipment is placed. The One-Hole test apparatus is adjusted at 45 degrees for the right-handed subjects.

The following instructions were given to the subject: "I want to see how many pins you can insert in that hole in one minute. You will have a total of seven trials, each lasting one minute, with five seconds rest between each trial, in which time if you get your fingers wet by perspiration, dry them with this paper tissue. Let me show you exactly what to do;" the experimenter grasps the one-prepositioned pin, moves it, and positions it to the hole and reaches for the next pin.

Repeat 3 cycles. After that demonstration, asks the subject "Do you have any questions?". If he has some questions, the experimenter will answer all of them. After that, he tells the subject "Now I will tell you when to start and when to stop". The command is: "are you ready Start ..... Stop".

Proceed with the same command for each trial.

The scores counted for one-hole test were:

(1)   Number of pins inserted in first 30 seconds - lowest

(2)   "   - highest

(3)   Number of pins inserted in 60 seconds - lowest

(4)   "   - highest

(5)   Number of pins inserted in seven trials - total

(6)   "   - lowest

(7)   "   - highest

(8)   Time corresponding to grasp (seconds) - total

(9)   "   - lowest

(10)   "   - highest

(11) Time corresponding to position (seconds) - total

(12)   "   - lowest

(13)   "   - highest

Figure 16

Section of the one-hole test apparatus showing the path of the pin from the hole at the top (a) to the receiving pan at the bottom (b).
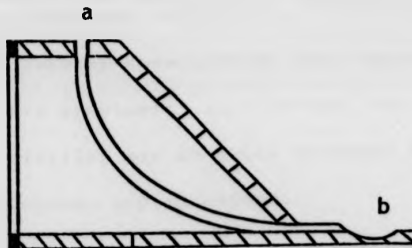
(from Salvendy G, 1968)

10.7 THE ADDING TEST

10.7.1. Background

It is possible that if impairment in the functions of the higher nerve centres (which could) appear in chronic low level exposure to lead it could be detected with tests of psychological abilities.

Fleishman (1960) has divided all psychological skills or abilities into three categories: perceptual, psychomotor and cognitive.

The adding test is a cognitive test and was chosen for performance tests as a decrement in performing this test could be related to changes in the higher nerve centres.

Adding tests resembling the present test have been used in the field of behavioural toxicology to detect decrements in the performance of subjects exposed to different levels of carbon monoxide (Shulte 1963, Johnson et al 1974) or to high body temperatures (Wilkinson et al,1963).

Shulte working on 49 healthy male adults exposed to mild carbon monoxide intoxication found that both the completion time and the number of errors in the arithmetic test were increased corresponding with the increasing level of carbon monoxide, and this could be corelated to alterations which appeared in the higher centres of the central nervous system in that area of the brain which controls some of the cognitive and psychomotor abilities. This alteration does occur at much lower levels of carboxy-haemoglobine than those which are necessary to produce subjective symptoms; furthermore, the degree of alteration in psychological abilities may be quite profound before any chemical signs of subjective symptoms are elicitted.

Johnson et al (1974) used an adding test, named Complex

Arithmetic, to test the behavioural performance capacity of workers

at possible excessive exposure to carbon monoxide.

The arithmetic task consisted of adding sets of five numbers

arranged in columns.

Each subject was limited in time to six minutes, and had been

instructed to complete as many additions problems as possible and as

accurately as possible. The number of problems completed within the

allotted time and the number of errors constituted the performance

measure for this task.

Wilkinson et al (1963) studied the performance of 12 normal

male volunteers on a battery of performance tests, among them an

adding test, at different levels of raised body temperature.

The adding test consisted in simple additions (five lines and five

columns of two-digit numbers) to be added and the answer written

down in each column and each row, and a grand total finally obtained.

The results obtained for the adding test showed a deterioration

with increasing body temperature. The results of the test suggest

that presence of a casual relationship between the performance and

body temperature i.e. the internal temperature of the body could be

responsible for change in performance.

Description of the test

The present adding test consists of ten squares, each square

having five lines, each line five two-digit numbers. The numbers were

taken from the tables of random numbers - Fowlie (1968).

The ten squares were put on to sheets of paper, each sheet comprising

five squares. The sheets were numbered and a total of four different
sheets constructed - Appendix No. 4.

10.7.2. Procedure

The subject was informed about the purpose of the test and asked
to add the numbers for each line and write down the total. After
that he was asked to add the five totals for the five lines of a square
and write down a grand total at the bottom of the square. After
finishing the first square the subject was asked to complete the square
No. 2 and so on in order. The name of the subject, the time of the
start and the time of the finishing of the test were noted by the
experimenter.

The scores of the test included the number of the errors and the
time taken to perform the test, in minutes.

10.8 THE TREMOR TEST

10.8.1. Background

The physiological tremor represents fine regular oscillations
which are superimposed on the electrical record of the contraction of
the voluntary muscle itself. Most normal people have some tremor
superimposed on their muscular activity which does not usually exceed
2% of the physiological range of amplitudes of movement of the limb.

The rhythm of the physiological tremor ranges between 8-12 Hz.
Lippold (1971).

Brumlick and Yap (1970) classified human tremor in: rest,
postural, intentional normal (physiological) and abnormal (pathologic).

The rest tremor is defined as that state in which there is no
voluntary innervation of the musculature, therefore a complete voluntary

relaxation is possible.

The theories have been advanced to explain normal rest tremor:
(1)   Brumlick and Yap (1970) in the ballistocardiographic hypothensis
hold that normal rest tremor is a cardiorespiratory phenomenon.
(2)   The microvibration hypothesis maintains that normal rest tremor
arises from the continual contraction of individual muscle fibres
(Brumlick and Yap 1970).
(3)   Lippold (1971) gave another hypothesis which sees the tremor
as a component superimposed upon normal voluntary muscle activity,
a "hunting" mechanism, a servo-mechanism in the reflex arc that controls
the muscle.

Postural tremor is equivalent to static tremor and refers to
that position when the part is voluntarily held still against the force
of gravity, as when the arm is held outstretched.

Intentional tremor (kinetic or movement tremor) is that when the
part of the body is moved purposefully towards a goal.

All normal tremors - normal rest tremor, normal postural tremor and
intentional tremor tend to show a large frequency component between 8-12 Hz.

In the abnormal tremor group, abnormal rest tremor which may be seen
in extrapyramidal disease such as Parkinsonism, has a frequency of 3-8 Hz.

Abnormal postural tremor is found in cases of alcoholism and
thyreotoxicosis where, while the frequency is within the normal range,
amplitude may be increased abnormally, - Bachrach and Bennett (1973).

Regarding the pathology of the tremor, Holmes (1960) showed that
the midbrain could play an important part in generating pathological
tremor when one of its parts, the central part (tegmentum) or the dorsal
part (tectum) is affected.

The tegmentum contains two large nuclei - substantia nigra, and red nucleus.

Holmes (1960) gave the hypothesis that lesions of substantia nigra are regarded as signalised by involuntary movements (presumably tremor) during voluntary movements.

This implies that under normal conditions, substantia nigra participates in the stablisation of voluntary movement.

The red nucleus has been described by Jenkner and Ward (1953) as a "tremorogenic" zone. Carey and DeJong (1954) indicate in their studies that tremor may be obtained by stimulating or destroying midbrain regions, between parietal regions and the red nucleus.

The physiological tremor could be affected by numerous factors such as: emotional strain, age, visual acuity, low temperature of the limbs, alteration in muscle length, fatigue etc. - Ward (1974).

The emotional strain could generate an increase in amplitude of the normal tremor and a hump in the spectrum at 10-12 Hz.

The age is correlated with the average frequency of tremor i.e. between 0-9 years old, the average frequency of tremor is 7.6 Hz., between 20-29 years old the average frequency of tremor is 10.4 Hz. and over 60 years old the average frequency of tremor is 8.3 Hz. - Ward (1974).

Visual acuity is related to tremor so that people with poor eyesight, especially long-sighted individuals (hypermetropes) show an unusually large amount of finger tremor.

Cooling the temperature of the limbs is accompanied by a reduction in the amplitude of physiological tremor.

Also, alteration in muscle length is corelated with physiological

tremor; when a muscle is stretched under a load the physiological tremor is accentuated.

Another factor could be fatigue, i.e. during fatigue the muscle exhibits a slight rise in tremor frequency and a marked increase in amplitude.

In the present work I included the testing of tremor as a measure of motor function in lead exposed people, because one of the classical early signs of neuromuscular disfunction, especially in cases of chronic lead intoxication is tremor.

Ravasini (1961) and Simpson et al (1964) mentioned tremor among the clinical symptoms in lead exposed people.

Wilson (1954) described among the pathology of motor system in lead poisoning the symptom of "tremor saturnimus", which is described by him as an irregular movement of interossei muscles and the distal group generally and of the lips, not distinguishable from analogus tremor seen in mercurialism. (In mercurialism the fingers tremble by themselves, at first is observed a deliberate movement, and it eventually becomes continuous with a frequency of 8-9 Hz. and is augmented when the limbs are used. This tremor responds to emotional stimuli).

Repko et al (1974) studied the tremor in four subgroups of lead workers with lead in blood below 70 ug/100 ml. and on four subgroups of lead workers with lead in blood above 70 ug/100 ml. The tremor was measured in conjunction with muscular strength, endurance and recovery.

The results showed that the four subgroups above 70 ug/100 ml. blood presented considerably more tremor than the other four subgroups.

All of the tremor measures of the exposed group were significantly
negatively correlated with ALA-D (amino-levulinic acid dehidratase).
In no case were these correlations significant for control workers.

The conclusion drawn by the authors was that there is a progressively
greater amount of tremor associated with levels of lead between 70-79 ug/100ml.
blood.

10.8.2. Equipment

The equipment for the tremor test was borrowed from The Royal Naval
Environmental Medicine Unit. The test equipment comprised:

Eight-channel portable magnetic tape recorder – S.E.Labs (EMI)
Ltd.. England

Oscilloscope

Paper Recorder

Accelerometer

Zero-ing potentiometer

Balance board

A scheme of the setting of the tremor equipment is given in Figure 19
(Page 134).

Posture tremor

An accelerometer was strapped to the index finger of the preferred
hand and the output amplified by a preamplifier. A power amplifier was
then used to enlarge the signal prior to it being fed into one channel
of an eight channel tape recorder and an oscilloscope.

Intention tremor

The subject had to press on a force lever using the second finger
of the preferred hand. The force required was 0.5 kg. weight and the
output was fed to a gauge for the subject to visually monitor his
performance to an eight channel tape recorder and an oscilloscope.

Figure 19 - Scheme of equipment used for testing tremor
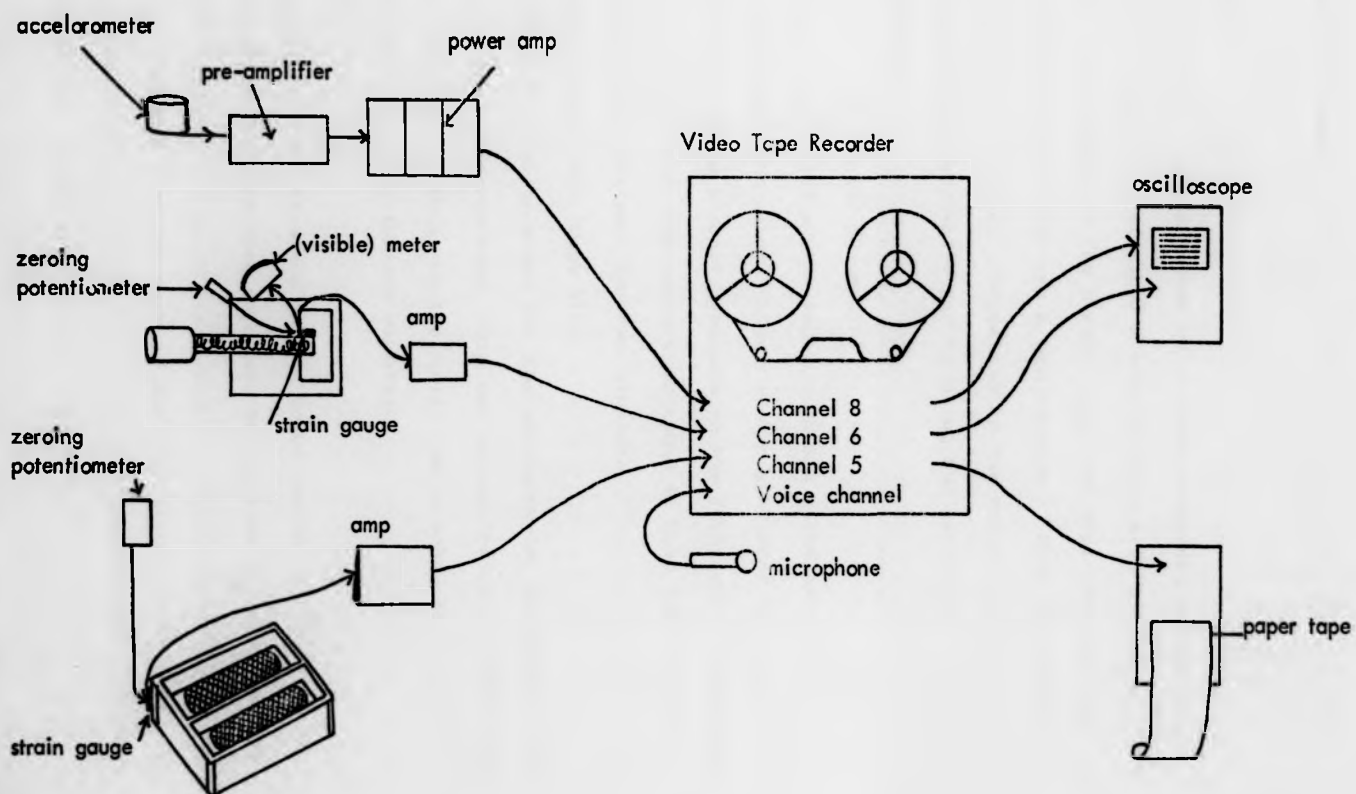
Prior to each experiment the force lever was calibrated with a 0.5 kg. weight.

Balance board

This part of the test consisted of a plate suspended at the four corners. To one corner was attached a strain gauge with a zero-ing potentiometer. The output of the strain gauge was amplified and fed to a multichannel tape recorder and a pen recorder. When the subject stood on the balance board any innequality in the weight carried by the side of the board was compensated for by using the zero-ing potentiometer.

10.8.3. Procedure

Intention tremor (Figure 20) (Page 110)

The subject is seated at the table with his right wrist hand on the table. He inserts the second finger of the preferred hand into the finger holder and applies a small pressure on the lever until the needle reaches the zero position; the subject is asked to keep the needle as still as he can and on the zero for two minutes.

Postural tremor (Figure 21) (Page 110)

The subject is asked to stand and the accelerometer is fixed to the index finger of his preferred hand. The arm is outstretched at the level of the eyes pointing to a point on the wall. He is asked to keep this position as still as he can for two minutes.

Balance board (Figure 21)

The subject is asked to stand on the board keeping as still as he can for two minutes with the eyes open and for another two minutes with the eyes shut.

The parameters measured for each of the four tremor (postural, intention, balance board, eyes open and eyes shut) represented a number of 64 variables; each of these variables represents the mean value of power over a spectrum of frequency of 0.5-32 Hz. in steps of 0.5 Hz

i.e. variable 1 = spectrum 0-0.5 Hz., variable 2 = spectrum 0.5-1 Hz.
and so on until variable 64 = spectrum 31.5-32 Hz. A total of 256
variables resulted in the four tremors.

10.9 NERVE CONDUCTION VELOCITY

10.9.1. Background

Nerve conduction velocity represents the speed at which the
nerve impulse travels along a nerve. The measure of this velocity
is one of the neurophysiological techniques introduced into the field
of occupational medicine for the purpose of revealing certain types
of disturbances within the nervous system produced by toxic substances
in the work environment. For example, in the present context, that
of lead poisoning, the classical symptom-paresis of the radial nerve
leading to wrist drop, practically belongs to history, but some workers
may still complain of numbness, cramps, pins and needles and pain in
their limbs, and 1 hoped to study the significance of these early
symptoms against the nerve conduction velocity changes if any, in
lead workers.

In the chapter on toxic effects of lead on the nervous system
9.2, the literature concerning work on nerve conduction velocity in
lead poisoning was reviewed (section 9.2.3.5.4.). It is known, Best
and Burke (1955) that a peripheral nerve is comprised of a bundle of
axons, the axon being associated with a single nerve cell or neuron
(Figure 22) (Page 137). The nerve cell, either motor or sensory, consists of
a cell body, a series of short processes known as dendrites and the axon.

Figure 22 - The anatomy of a peripheral nerve
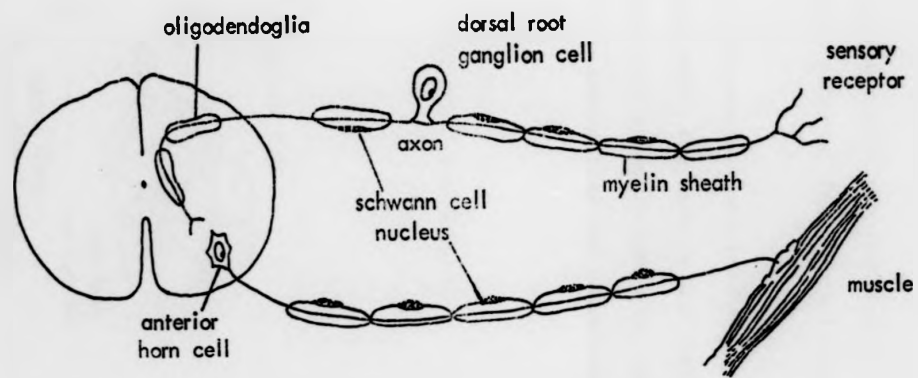
THE ANATOMY OF A PERIPHERAL NERVE

(from Scala R.A. 1976)

The body of the peripheral motor nerve cell is found in the anterior portion of the spinal cord while the sensory nerve cell body is in the dorsal root ganglion.

The cell body supports the function of the axon by maintaining a flow of nutrient material from the cell body down through the axon itself.

In a motor neurone the receptive segment includes the dendrites and the cell body while the axon is the conductile segment.

A motor axon terminates in the motor end plate of the muscle and is responsible for stimulating the contractual process of the muscle. (Figure 23):-

Figure 23 - The scheme of a motor unit

spinal cord

spinal nerve

cell body
of neuron

nerve fibre
(axon)

muscle fibres
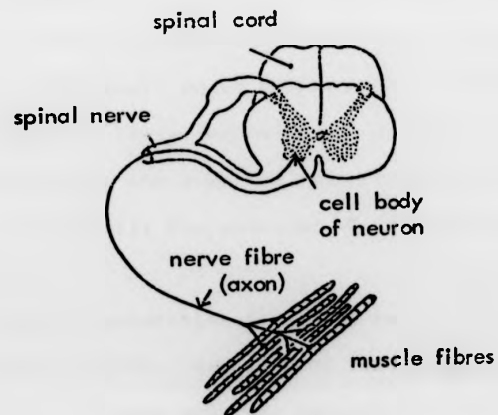
(from Smorto P.M. and Basmajian J.V. 1972)

Usually all nerve fibres over 2 microns in diameter are sheathed with a fatty substance known as myelin. The sheath is periodically interrupted with gaps and nodes of Ranviery. Some sensory axons have no myelin sheath and are relatively slow conducting. All axons, whether motor or sensory and whether sheathed with myelin or not are surrounded by Schwann cells.

Interference with the structural maintenance program of the neuron may result in a degeneration of a distal portion of the axon. This degeneration is followed by a loss of the property of impulse transmission. If the damage is confined to myelin, the only result will be a reduced conduction speed and remyelination can occur without any other loss of function. This injury process is relatively rapid and changes are quite evident within two to three weeks - Scala (1976).

Transsection or other severe damage to the peripheral nerve fibre (axon) itself results in a loss of function of that nerve cell.

Subsequent to this type of damage is a pattern of anatomic changes known as Wallerian degeneration ., in which the axon and the myelin break up into small ovoid bodies which are later phagocytized.

Repair of these severe axonal damage is slow because both regeneration of the axon and remyelization must occur.

Schematically the sequence of these events can be seen in Figure 24 (Page 140).

Axonal regeneration is at the rate of about one millimeter per day — Scala (1976). Recovery of the integrity of a peripheral nerve is possible because numerous Schwann cells will efficiently remyelinate the developing axon.

Figure 24 - The sequence of events in axonal neuropathy

normal early late regeneration
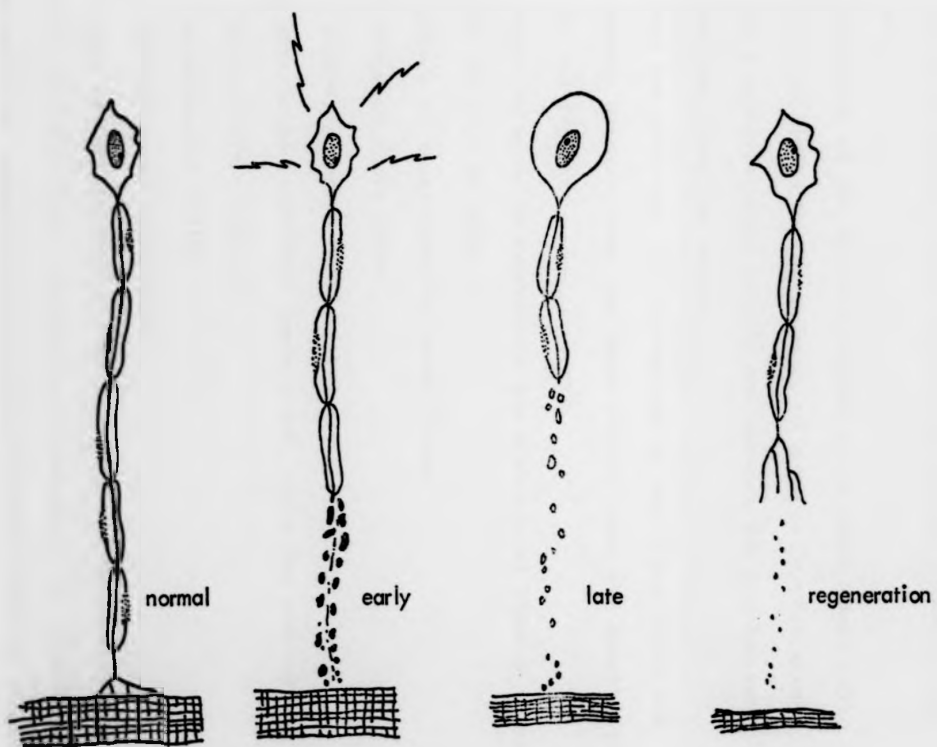
(from Scale R.A. 1976)

This cannot occur in the central nervous system but only in
the peripheral nervous system.

Regarding the lead poisoning, the histological changes in
nerves have been reviewed in Chapter 9.2.1. of the present work,
from which it was concluded that the type of the neuropathy and
the pathology of the myelin sheath in this particular poisoning are
still unclear.

On transmission of the nervous impulse it is known (Best 1955)
that a stimulus initiates the propagation of a nerve impulse which
gives rise to a negative spike locally and spreads the impulse wave
in both directions along the nerve.

Therefore the potential can be recorded at any point along the
motor and sensory pathway, from the nerve itself, from the muscle fibre,
from the skin and from the cerebral cortex.

The conduction velocity represents the distance an impulse travels
along a nerve per unit of time.

The presence of three specific nerve fibres –

    the efferent nerve fibre

    the sensory afferent muscle fibre

    the skin sensory afferent nerve fibre, allow the testing of:

        motor nerve conduction

        monosynaptic reflex

        sensory nerve conduction.

Motor nerve conduction velocity of a nerve could be obtained by
stimulating the nerve at the two points, the proximal and the distal
part of the nerve and measuring the distance between these two points.
The time taken by the impulse travelling between these two points is the

difference between the two times. The formula for determining
conduction velocity in meters per second is: the distance in mm.
divided by the time in milliseconds - in other words, after stimulation
at two points two action potentials are obtained; in each case the
artifact of the stimulus and the take-off of the action potential is
called the latency time or conduction time.

By subtracting the time of the distant stimulus from that of the
proximal stimulus we obtain the time required for the nerve impulse to
travel the segment of the nerve between the two points of stimulation.
The length of those segments (distance) divided by the differences in
latencies (time) gives the velocity according to formula:

$$Velocity = \frac{Distance}{Time}$$

after Smorto and Basmajian (1972).

The normal motor conduction velocity of the peripheral nerves
varies in normal adult individuals. From the Table 7 (page 143) we can
see that for the median nerve the motor conduction velocity could be
ranged 47-70 m/sec., for ulnar nerve 47-66 m/sec., for radial nerve
45-82 m/sec., and for peroneal (lateral popliteal) nerve 45-56 m/sec.

The normal motor conduction velocity varies with the temperature
of the skin and with the age of the subject.

The influence of temperature on nerve conduction has been studied
by Henriksen (1956) who found that the mean variation in conduction
velocity recorded in human ulnar nerves may reach a value of 2.4 m/sec.
per degree (centigrade) change in temperature. This means that during
a clinical standard examination an error of up to 6 m/sec. may occur if
care is not taken to warm up the limb tested, between 32-33.5°C.

Nerves tested

Source	Median				Ulnar				Radial				Peroneal			
	Mean	Range	SD	SE	Mean	Range	SD	SE	Mean	Range	SD	SE	Mean	Range	SD	SE
Johnson-1960	53.0		6.1		55.1		6.4						50.0		7.2	
Henriksen-1956	58.5	53-64.3			59.1	49-65							51.5	45-56		
Thomas-1960					60.4	47-73	5.4						51.0		3.3	
Vasilescu-1968	56.8	49-69	2.8		57.3	49-66	2.9									
Shubert-1967									78.1		6.0	1.0				
Gassel-1964									72.0		6.0	1.4				
Norris-1953					55.6		2.0									
Lawrence-1961	59.0			0.6	62.4			0.7					47.1			0.5
Trojaborg-1964	56.0			0.9	56.0			0.9					49.6			0.9
Trojaborg-1969									70.0			1.4				
Mavor-1966	64.3	59-70			60.0	56-62										
Thomas-1959	57.2			0.9	56.2			0.7					49.7			1.3
Bolzani-1955					54.0	46-63										
Gilliat-1960					54.5	46-65	5.5									
Rolak-1965					55.7		0.8									
Skillman-1961					56.4		1.1									
Mayer-1963	59.5			0.7	58.9			0.4					49.5			1.0
Bauer-1965	57.2			1.5	58.2			1.8					53.0			1.9
Jebsen-1966	56.4			0.6	59.7			0.6	58.4	45-82	6.7		47.3	40-57	4.3	0.5
Fatto-1960					66.7			0.9								
Thiers-1967	58.7			0.6	55.9			0.7					48.2			1.2

The influence of age on conduction velocity in nerves has been studied by few authors.

Thomas and Lambert (1968) showed that conduction velocity was slower in elderly subjects and in children up to five years of age.

Seppalainen et al (1975) reported that most motor conduction velocities slow down by about 1 m/sec. for every ten years of age between 20 and 60 years.

Norris et al (1953) who studied age changes in the maximum conduction velocity of motor fibres of human ulnar nerve found that conduction velocity decreases with increasing age in all segments of nerve ($P < 0.001$ between same age group).

This reduction cannot be attributed to nerve fibre degeneration or to temperature differences in the arm but may result from vascular changes in the nerve trunk and alterations in the nerve metabolism associated with membrane permeability.

Wagman and Lesse (1952) reported on relationship between motor nerve conduction velocity of ulnar nerve and the age of a person and found that over 60 years of age the conduction velocity was reduced by about 10%.

10.9.2. Equipment

The basic standard of equipment for recording the nerve conduction velocity consists of stimulating and recording apparatus and stimulating and recording electrodes.

The apparatus used in the present work was a Medelec M S 7 two-channel Electromyograph which is a portable unit used for a wide range of electrophysiological measurements (Figure 25) (Page 111). The portable, dual channel electromyograph type MS7 employs plug-in modules.

The unit incorporates a flat faced CRT which provides a large, bright dual trace display on a 10cm x 8cm. screen, an internal graticule simplifies measurement free of parallax errors. Comprehensive sweep velocity controls enable timebase velocity to be adjusted over the range 0.5 to 500ms./cm. and time calibration signals are provided to check the accuracy of calibration. A constant voltage nerve stimulator with a direct reading conduction time indicator enables response times to be measured over the range 0-100ms.

A built-in loudspeaker may be switched to either input channel, permitting audio monitoring of the subject signal. A fibre-optic Recorder type FOR-7 was interfaced directly with the MS 7 and provided records of the displayed traces on direct print paper. Interconnections between the two units were made via multi-core cable; viewing on the MS7 display is unimpaired (Figure 26) (Page 111).

Display area 10x8cm.

Timebase - free running or triggered by stimulator

Sweep velocity switched 1ms/cm.

Stimulus frequency 1/sec.

Stimulus duration 0.1ms.

Stimulus amplitude 0-450 volts.

Output impedance: 200.

The electrodes

The stimulating electrodes are the button electrodes, silver discs of one cm. diameter adapted to a plastic plate of dimensions 6.5/4cm. (Figure 28) (Page 112). The plastic plate allows for free and quick reallocation of electrodes towards the point of the maximum stimulation.

The recording electrodes are of clip spring type, they pick up the electrical potential and relays it to the amplifier for magnification (Figure 27) (Page 112). The pulse is of 0.1m.sec. duration and of 100-150 volts usual, going up to 300-400 volts. The skin temperature was measured with a Light Laboratory thermistor thermometer (Figure 26) (Page 111).

10.9.3. Procedure

The ulnar nerve conduction

The subject is lying on a couch, with the elbow and wrist fully extended and the shoulder placed in ten degrees of abduction. The electrodes used for stimulating the ulnar nerve are placed directly over the nerve at the wrist as the nerve passes from its' course along the medial volar aspect of forearm to the hamate bone.

The recording electrodes pick up the synchronous electrical activity in the abductor pollicis brevis muscle following ulnar nerve stimulation. The motor point of this muscle is often apparent as a slight depression just distal to the mid-part of the thenar eminence. The indifferent electrode is placed at the base of the thumb. A large plate electrode, coated with electrode jelly is taped to the skin of the hypothenar emience and connects the subject to the ground and so reducing the fifty cycles interference.

Securing the thumb in the position of the extension is necessary to reduce any voluntary movement artefacts to a minimum, i.e. the experimenter held the subject's thumb in such a position whilst making the recording.

A gradually increasing amplitude of the stimulus was applied until the supramaximal stimulation of the ulnar nerve was attained. This was seen on the oscilloscope as the point when no further increase in the electromyography action potential occurs. A permanent record was then taken.

After that a second pair of stimulating electrodes were placed over the ulnar nerve as it passes through the ulnar groove of the humerus. The procedure of stimulating was the same. For the elbow-wrist segment of the nerve the difference in the latencies of the response to stimulation is divided into the distance between the two sites of the stimulation, providing the velocity in m/sec.

The median nerve conduction

The stimulation points are at the wrist and at the elbow. The recording electrodes are placed over the opponens pollicis or the abductor pollicis brevis muscle. The procedure is the same as for the ulnar nerve.

The 8 parameters resulted from nerve conduction velocity study were:

1,2 Maximum motor conduction velocity (metres/second) in the dominant arm for ulnar nerve and median nerve

3,4 The amplitude of the muscle action potential (mv) following stimulation at the elbow in dominant arm for ulnar nerve and median nerve

5,6 The amplitude of the muscle action potential (mv) following stimulation at the wrist in dominant arm for ulnar nerve and median nerve

7,8 The percentage of amplitude of muscle action potential elbow/ wrist (%) in dominant arm for ulnar nerve and median nerve. The

percentage amplitude was calculated from this equation:

$$\frac{\text{amplitude of proximally produced muscle action potential (V)}}{\text{amplitude of distally produced muscle action potential (V)}} \times 100 = \text{percentage amplitude}$$

10.10 BIOCHEMICAL TESTS

The measurement of blood lead, urinary lead and amino levulinic acid in urine was carried out by the National Occupational Hygiene Service Laboratories - Manchester.

The blood and urinary lead were measured by the method of Hoschek R. and Schittke H.J. (1973) using single tube dithizone technique.

The amino levulinic acid in urine was measured by the method of Davis J.R. and Andelman S. (1967) using the Davis Urinary ALA test as supplied by Bio-Rad Laboratories.

11. RESULTS

11.1 Introduction

In the the chapter of methodology (10.2) the number of the population tested and the distribution by the departments for the exposed people was shown in Tables No. 4 and 5.

The exposed and control groups were matched within each factory in terms of sex, race, age, weight, height, education, geographic location and length of employment for the exposed people and controls.

For different reasons i.e. holiday, sick leave, night shift, it was impossible to collect a complete set of data from some of the subjects;

therefore.   , the analysis was computed on the basis of available
data and a notation have been made as to the number of observations
included in each analysis.

The information collected from the questionnaire and from the
forms filled for each psychomotor test, tremor and nerve conduction
velocity was transferred to five punch cards for each of the subjects
tested, on a coding schedule with the following sections:

Population physical characteristics

Biochemistry tests

Performance tests

Tremor test

Nerve conduction velocity.

The variables entered under the above sections are listed in the Appendix
No. 1. Out of 541 variables a number of 290 were summarised. In
analysing the results the statistical significance is claimed when the
probability of the results occurring by chance is equal to or less than
0.05.

11.2 Population physical characteristics

In this section the age, weight, height and length of exposure for
people exposed to lead and length of employment for the controls were
analysed; (for convenience the name used will be length of employment
for both groups).

The age distribution, mean age, standard deviation, lowest and
highest value for age are shown in the Table No. 8 (Page 150) and in
Figures 29-34 (Page 151-152).

TABLE 8 The mean, standard deviation, lowest and highest age

	Number	Mean	Age (years) Standard deviation	Lowest	Highest
Exposed					
Factory I	67	39.8	9.1	23	60
Factory II	30	43.4	7.3	31	57
Factory I and II	97	40.9	8.7	23	60
Controls					
Factory I	79	38.8	9.3	23	58
Office Staff	49	38.2	9.7	23	57
Manual Workers	30	39.7	8.8	24	58
Factory II	30	42.8	10.5	23	58
Factory I and II	109	39.9	9.8	23	58

FIG.29

%

45 —
40 —
35 —
30 —
25 —
20 —
15 —
10 —
5 —
0 —

FIG.30

%

45 —
40 —
35 —
30 —
25 —
20 —
15 —
10 —
5 —
0 —

FIG.31

%

45 —
40 —
35 —
30 —
25 —
20 —
15 —
10 —
5 —
0 —

FIG.32

%

45 —
40 —
35 —
30 —
25 —
20 —
15 —
10 —
5 —
0 —

PERCENTAGE DISTRIBUTION OF AGE

FACTORY I
EXPOSED
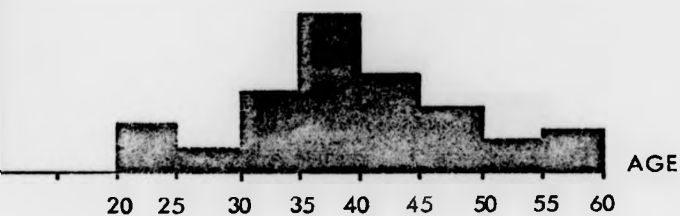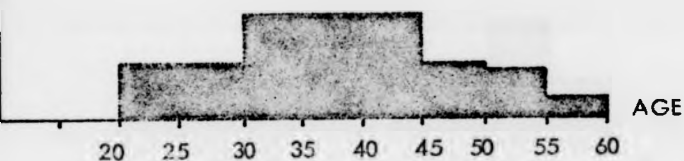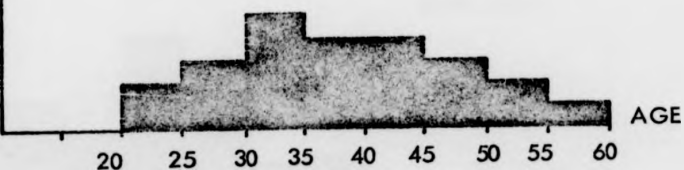
AGE

20 25 30 35 40 45 50 55 60

FACTORY I
CONTROLS

AGE

20 25 30 35 40 45 50 55 60

FACTORY I
OFFICE CONTROLS

AGE

20 25 30 35 40 45 50 55 60

FACTORY I
MANUAL CONTROLS

AGE

20 25 30 35 40 45 50 55 60

PERCENTAGE DISTRIBUTION OF AGE

FIG.33

FACTORY II
EXPOSED

FIG.34

FACTORY II
CONTROLS

PERCENTAGE DISTRIBUTION OF LENGTH OF EMPLOYMENT

FIG.35

FACTORY I
EXPOSED

FIG.36

FACTORY I
CONTROLS

PERCENTAGE DISTRIBUTION OF LENGTH OF EMPLOYMENT

FIG. 37

FACTORY I
OFFICE CONTROLS

FIG. 38

FACTORY I
MANUAL CONTROLS

FIG. 39

FACTORY II
EXPOSED

FIG. 40

FACTORY II
CONTROLS
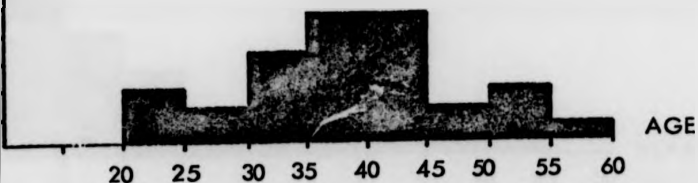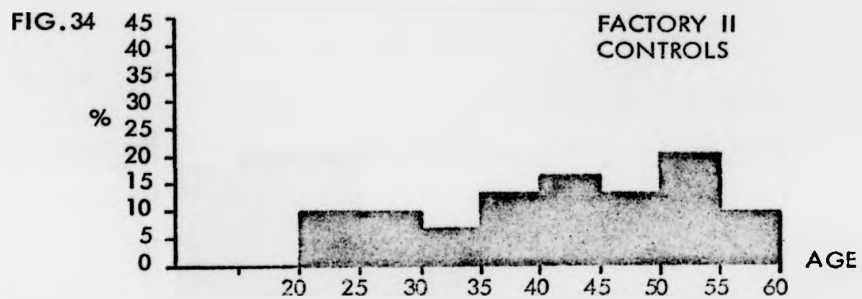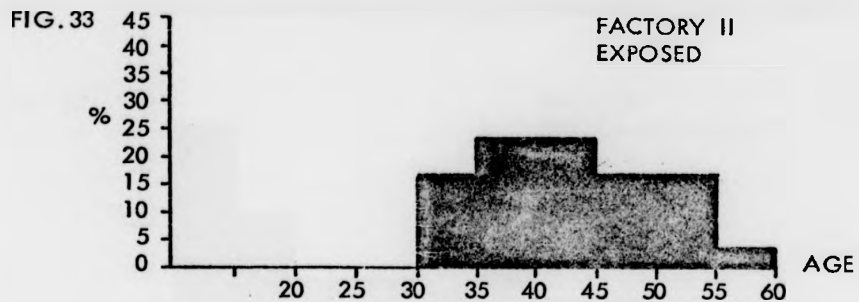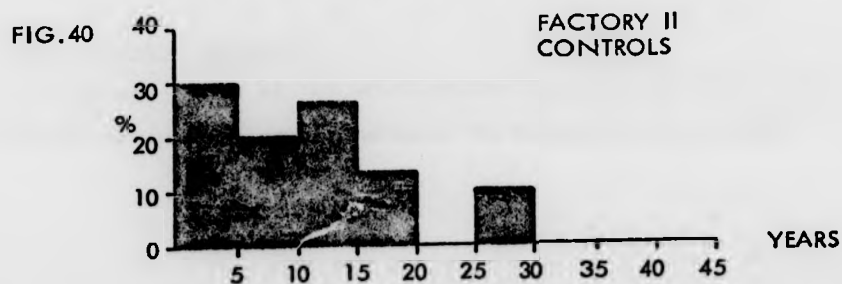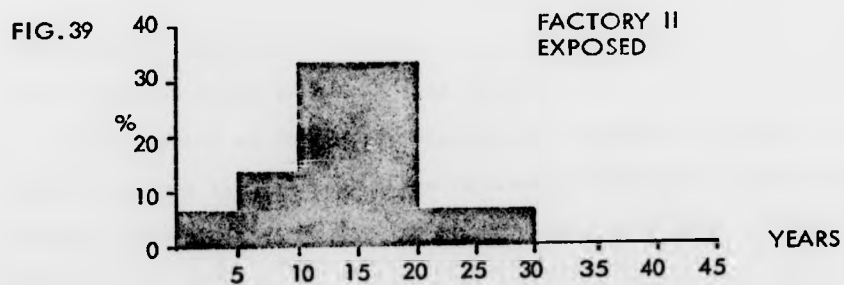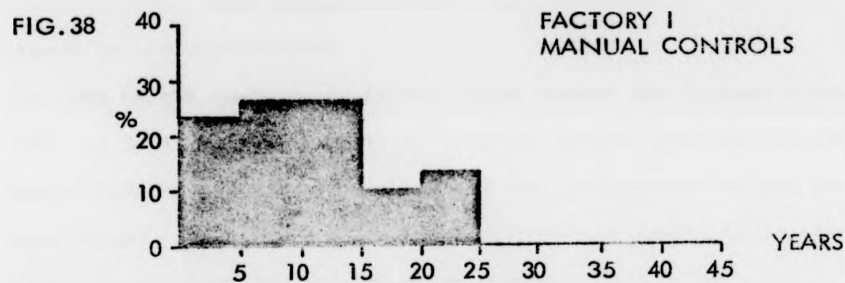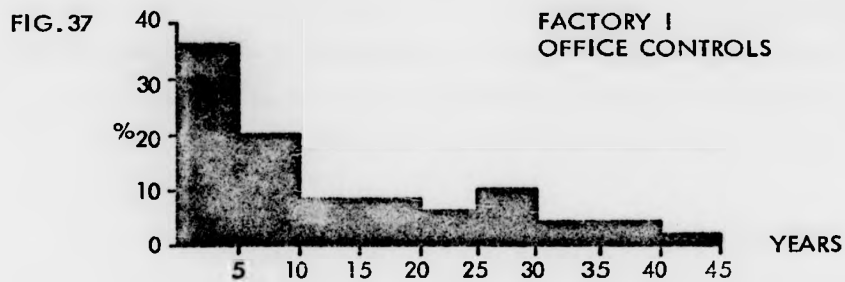
There is little difference in the average age between exposed workers and controls of the combined factories but not significant for the present work; in Factory I the workers tended to be slightly younger than those in Factory II, particularly with respect to the office staff controls.

The weight mean, standard deviation, lowest and highest value are shown in Table 9 (Page 155). The small difference between exposed and controls of the combined factories is of no significance in regard to the present work.

The height mean, standard deviation, lowest and highest value are shown in Table No. 10 (Page 156) There is little difference in average height between the exposed workers and the controls in the two factories considered; the Factory I office staff controls tended to be slightly taller on the average than the other groups.

The length of employment distribution, mean, standard deviation, lowest and highest number of years are shown in the Table Nr.11 (Page 157) and in Figures 35-40 (Pages 152 and 153).

The majority of the people studied are included in the group of employment from 1-15 years. There is a small difference between means of exposed and controls from Factory II, but not significant for the present study.

11.3. Clinical Symptoms

Section III-VI of the questionnaire (Appendix 3) deals with subjective symptoms of lead effect. In designing the present

TABLE 9 The mean, standard deviation, lowest and highest weight

	Number	Mean	Weight (kg.) Standard deviation	Lowest	Highest
Exposed					
Factory I	64	76.6	9.5	50	95
Factory II	29	76.1	10.0	61	96
Factory I and II	93	76.4	9.5	50	96
Controls					
Factory I	73	74.6	9.0	55	97
Office Staff	45	74.9	8.0	59	97
Manual workers	28	74.3	10.5	55.5	95
Factory II	29	74.2	8.2	58	88
Factory I and II	102	74.5	8.7	55	97

TABLE 10 The mean, standard deviation, lowest and highest height

		Height (cm)		
	Number	Mean	Standard deviation	Lowest	Highest
Exposed					
Factory I	64	173.5	6.5	161	190
Factory II	30	173.4	6.3	163	185
Factory I and II	94	173.5	6.4	161	190
Controls					
Factory I	77	175.0	6.8	158	188
Office Staff	47	176.0	6.4	161	187
Manual workers	30	173.4	7.2	158	188
Factory II	30	172.7	7.6	152	195
Factory I and II	107	174.3	7.0	152	195

TABLE 11 The mean, standard deviation, lowest and highest length of employment

| | Number | length of exposure | | | |
		Mean	Standard deviation	Lowest	Highest
Exposed					
Factory I	67	13.1	7.4	2	32
Factory II	30	14.7	5.6	5	29
Factory I and II	97	13.6	6.9	2	32
Controls					
Factory I	79	12.6	10.0	1	41
Office Staff	49	13.4	11.5	1	41
Manual workers	30	11.3	7.0	2	25
Factory II	30	11.4	7.7	1	30
Factory I and II	109	12.3	9.4	1	41

questionnaire I followed the pattern used in a similar work (Heather, Mitran and Crockford, 1976) and improved it from models of questionnaires used in epidemiological studies in the TUC Institute of Occupational Health, London. The symptoms of lead poisoning are . . protean ; it is difficult in cases of subclinical lead poisoning to determine which of the subjective symptoms, if any, belong really to a lead exposure or to other causes - age, stress, pollution etc.

I consider that one's experience in clinical questioning could contribute in attributing the symptoms to lead exposure than to other causes.

In this study only the symptoms which had no other explanation for a particular subject (no other known disease) had been taken into account. The attention in asking questions had been given to nervous system as related directly with present work, but the disturbances from other organs were questioned too, according to the subjective symptoms mentioned in the literature on lead poisoning (section 9.2.3.3.2).

It must be mentioned that an objectively clinical examination of the subjects was not practically possible at the time of the testing, so general information about the health of the subject was obtained by questioning him about the subjective symptoms. If some unusual subjective symptoms related to lead poisoning were reported, the medical records should have been consulted to relate them with the subject's objective examination which is carried out by the factory doctor as a routine. The questions on subjective symptoms were interpreted by the author only qualitatively and not quantitatively: no statistical analysis was considered necessary.

Table No. 12 (Page 160) shows the clinical findings in both factories. It appears that exposed subjects from Factory I are more irritable, more nervy, quarrel more at work or at home, than exposed subjects from Factory II; the same situation is in the controls group which leads to the question if these symptoms could be attributed to lead or to work environmental factors - noise, dust, temperature etc.

Factory I exposed subjects suffer more from insomnia than the exposed of Factory II and the same situation is regarding vertigo; 16.5%-19.9% of the subjects, respectively in Factory I and II suffer from headache, which is frequent during the week and less at the weekend; the situation being similarly in controls, again the question of attributing it to lead exposure or to environmental factors arises.

A group of symptoms which present much much interest for the present study i.e. numbness in arms and legs, difficulties in running, walking, grasping objects, cramps in legs in the day or night, being a subjective expression of an incipient peripheral neuropathy have been investigated. In Factory I exposed 25.3% suffer from numbness in arms and legs and in Factory II, 26.6%; 22.4% exposed from Factory I suffer from difficulties in running, walking, grasping and lifting objects against 3.3% in Factory II; 13.3% exposed in Factory II complain of coldness in the hands against only 4.5% exposed in Factory I; 22.5% exposed in Factory I suffer from cramps in the legs and 26.6% in Factory II against 19% controls in Factory I and 16.6% in Factory II.

The symptoms of eyes-blurred vision, strabism or myopia could be attributed more to age than to lead exposure.

TABLE 12   Subjective clinical symptoms found in exposed
and control subjects

Symptoms	Exposed Factory I		Factory II		Controls Factory I		Factory II	
	No.	%	No.	%	No.	%	No.	%
Change in temper -more irritable & nervy	14	20.9	2	6.6	10	12.7	2	6.6
Quarrel more								
at work	11	16.4	1	3.3	6	7.6	2	6.6
at home	12	18.0			10	12.7		
Sleep difficulty - time to get to sleep(mean)	11		11		11		11	
Insomnia	10	14.9	2	6.6	3	5.8		
Hours of sleep(mean)	6		7		7		7	
Headache								
morning	1	1.5			1	1.3		
end of day	4	6.0			3	3.8	1	3.3
during week	5	7.5	5	16.6	1	1.3	1	3.3
Weekends	1	1.5	1	3.3	1	1.3	1	3.3
Dull	6	9.0	4	13.3	3	3.8	1	3.3
Throbbing	5	7.5	2	6.6	3	3.8	2	6.6
Vertigo								
at work	10	14.9	3	10.0	5	6.3	2	6.6
outside work	1	1.5			5	6.3		
all time	2	3.0			1	1.3		
Numbness in arms and legs								
constant	9	13.4			1	1.3		
occasionally	8	11.9	8	26.6	5	6.3		

	Exposed				Controls			
	Factory I		Factory II		Factory I		Factory II	
	No.	%	No.	%	No.	%	No.	%
Difficulties in								
running	5	7.5	1	3.3	4	5.1		
walking	3	4.5			3	3.8		
grasping &								
lifting	7	10.4			7	8.9		
Coldness in								
hands	3	4.5	4	13.3	3	3.8		
Cramps in legs								
day - constant								
- occasionally	4	6.0	2	6.6	5	6.3		
night -constant	1	1.5						
-occasionally	10	15.0	6	20.0	10	12.7	5	16.6
Loss of weight	1	1.5	1	3.3	1	1.3	1	1.3
Diarrhoea	4	6.0			3	3.8		
Constipation	1	1.5						
Nausea	2	3.0						
Abdominal pain	5	7.5						
Blurred vision	10	15.0	1	3.3	3	3.8		
Any sight defect	7	10.4	1	3.3	3	3.8		

NOTE: In the present and following tables, blank spaces mean zero results.

| | Exposed | | Controls | |
| | Factory I | Factory II | Factory I | Factory II |
	No. %	No. %	No. %	No. %
Difficulties in				
running	5 7.5	1 3.3	4 5.1	
walking	3 4.5		3 3.8	
grasping &				
lifting	7 10.4		7 8.9	
Coldness in				
hands	3 4.5	4 13.3	3 3.8	
Cramps in legs				
day - constant				
- occasionally	4 6.0	2 6.6	5 6.3	
night -constant	1 1.5			
-occasionally	10 15.0	6 20.0	10 12.7	5 16.6
Loss of weight	1 1.5	1 3.3	1 1.3	1 1.3
Diarrhoea	4 6.0		3 3.8	
Constipation	1 1.5			
Nausea	2 3.0			
Abdominal pain	5 7.5			
Blurred vision	10 15.0	1 3.3	3 3.8	
Any sight defect	7 10.4	1 3.3	3 3.8	

NOTE: In the present and following tables, blank spaces mean zero results.

11.4 Smoking Habits

The smoking habits results are given in Table 13 (Page 162).
Factory I exposed people seem to be heavier smokers than that of
Factory II; 77.1% of the exposed in Factory I are smokers against
56.6% in Factory II; from these 10.4% are smokers Grade I in Factory I
against 43.3% in Factory II; 56.7% are smokers grade I and II of
the exposed Factory I and only 13.3% of Factory II.   The controls
does not present much difference as the total number of smokers in
in both factories, but the smokers in Factory I seem to be heavier
smokers than in Factory II.

Reported to the whole group of exposed and controls, a large
number of people had given up smoking in controls 56.4% than in
the exposed 31%.

11.5 Drinking Habits

The drinking habits results are given in Table No. 14 (Page 163).
In the Factory I 91.1% of the exposed are drinkers against 69.9% in
Factory II.   Regarding the grade of drinking, only 40% of the total
exposed are in Grade 1 in the Factory I, 47.8% in grade II and 3%
in the group of moderate spirit drinkers;   in Factory II 63.3%
of the total exposed are in grade I and 6.6% in grade II.

The controls follow the same pattern in both groups; 94.9% of the
controls are in grade 1 in the Factory I, 22.8% in grade II, 1.3% in
grade III and 5.1% are moderate spirit drinkers;   in the Factory II
50% of the total controls are in grade I and 16.6% in grade II.

TABLE 13 Smoking habits in exposed and control subjects

Degree of smoking	Exposed				Controls			
	Factory I		Factory II		Factory I		Factory II	
	No.	%	No.	%	No.	%	No.	%
Grade I 1-14 cigarettes/ day up 3oz. tobacco/week	7	10.4	13	43.3	15	19.0	12	40.0
Grade II 15-24 cigarettes/day up 6ozs./tobaco week	20	29.9	4	13.3	17	21.5	5	16.6
Grade III over 25 cigarettes/day over 6ozs/tobacco/ week	18	26.8			9	11.4		
TOTAL		77.1		56.6		51.9		56.6
Age-started mean	16.1		15.5		17.1		14.8	
Gave up smoking	10	14.9	5	16.1	16	20.3	5	16.1

TABLE 14 Drinking habits in exposed and control subjects

	Exposed				Controls			
	Factory I		Factory II		Factory 1		Factory II	
Degree of Drinking	No.	%	No.	%	No.	%	No.	%
Grade I								
1-14 pints beer/week	27	40.3	19	6?.3	52	65.8	15	50.0
Grade II								
15-50 pints beer/week	32	47.8	2	6.6	18	22.8	5	16.6
Grade III								
over 50 pints beer/week					1	1.3		
Spirit drinkers 1-3 whiskies/week	2	3.0			4	5.1		
TOTAL		91.1		69.9		94.9		66.6
Non-drinkers	6	8.9	9	50.0	4	5.1	10	33.3

11.6 Biochemical tests

In the chapter 10 section 10.10 the methods used in measuring the blood lead (BL), urinary lead (UL), and amino-levulinic acid in urine (ALA) have been described.

The blood lead mean, standard deviation, lowest and highest values are shown in the Table 15 (Page 165). There is little difference in the average blood value between the exposed groups. The control group from the Factory II had an average blood lead higher than the controls of Factory I but still within the normal range according to the present standards of 20-40 micrograms/100ml. blood. This difference could be attributed to the fact that the controls of Factory II come from the maintenance department only, and so could have come into unknown contact with lead for a short period of time at about the time of testing, and therefore their lead absorption, expressed as blood lead, increased. It must be mentioned that the selection of this group as controls was done on the basis of their blood lead test twelve months prior to the present study when their mean blood lead had been 27.1/micrograms/100ml. with a standard deviation of 5.9 (Table 16) (Page 166). The elevation in blood leads of the control group from Factory II is mainly due to three individuals, an observation which fits the above explanation.

The urinary lead means, standard deviations, lowest and highest values are given in the table No. 17 (Page 167). A difference could be seen for the Factory II controls. This could be due to the same factor as for the above blood lead. It must be stressed that the people who show a bigger value for urinary lead, do not show the same tendency for blood lead or for ALA.

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The urinary lead means, standard deviations, lowest and highest values are given in the table No. 17 (Page 167). A difference could be seen for the Factory II controls. This could be due to the same factor as for the above blood lead. It must be stressed that the people who show a bigger value for urinary lead, do not show the same tendency for blood lead or for ALA.

TABLE 15 The mean, standard deviation, lowest and highest blood lead

| | | Lead (ug/100ml) | | | |
	Number	Mean	Standard deviation	Lowest	Highest
Exposed					
Factory I	67	51.9	11.2	22	79
Factory II	30	50.0	10.8	32	68
Factory I and II	97	51.3	11.0	22	79
Controls					
Factory I	78	26.7	9.1	13	41
Office staff	48	25.5	9.2	13	41
Manual workers	30	28.8	8.6	16	43
Factory II	30	31.5	8.4	18	43
Factory I and II	108	29.3	10.7	13	43

TABLE 16 The mean, standard deviation, lowest and highest blood lead values for Factory II controls over a period of 12 months prior to the present study

Subjects	Number	Mean	SD	Lowest	Highest
Factory II controls	28	27.2	3.9	18	30

TABLE 17 The mean, standard deviation, lowest and highest urinary lead

	Number	Mean	Standard deviation	Lowest	Highest
			Urinary lead (micrograms/litre)		
Exposed					
Factory I	66	70.1	35.8	6	209
Factory II	30	78.4	50.5	18	195
Factory I and II	96	72.7	40.9	6	209
Controls					
Factory I	77	25.1	21.3	5	76
office staff	47	27.5	35.6	5	76
Manual workers	30	21.2	11.4	10	72
Factory II	30	36.2	15.2	11	83
Factory I and II	107	30.5	24.4	5	83

The amino-levulinic acid in urine means, standard deviations, lowest and highest values are given in Table 18 (Page 169). For this test, considered to be the most sensitive among the three biochemical tests performed for this work, no significant differences appeared among the means for the two factories.

Four workers out of ninety-seven exposed to lead in Factory 1 had a blood lead value between 70-79ug/100ml. blood. Their urinary lead and amino levulinic acid in urine were not concordant with blood lead values being under 450ug/litre and 3.2 mg ./litre respectively for urinary lead and ALA.

11.7 Performance Tests

The name and number of parameters registered for each of the performance tests had been indicated in the chapters of methodology sections 10.4 to 10.7. Out of 70 variables a number of 19 variables were summarised in Table 19 (Pages 170 and 171) where the results as means and standard deviations for each of performance test are given on the following five groups of subjects: Factory I - exposed, manual controls, office controls, Factory II - exposed and controls.

Four people in the Factory I had their blood lead between 70-79 ug/100ml. blood. Analysing the means and standard deviation for each of performance test in this group of four subjects, none of the values come different than that of the means and standard deviation of the whole group of the exposed in Factory 1. The differences seen in Table 19 (Pages 170 and 171) between groups are discussed in section 11.7.5., when the results on performance are more relevant, after the statistical analysis.

TABLE 18 The mean, standard deviation, lowest and highest amino-levulinic acid in urine

	Number	Mean	Standard deviation	Lowest	Highest
			ALA (miligrams/litre urine)		
Exposed					
Factory I	66	4.4	3.6	0.5	18.5
Factory II	30	3.6	3.2	0.2	15.5
Factory I and II	96	4.1	3.5	0.2	18.5
Controls					
Factory I	77	2.6	1.6	0.2	8.4
Office staff	47	2.5	1.7	0.2	8.4
Manual workers	30	2.6	1.5	0.3	7.6
Factory II	30	2.8	1.7	0.2	7.4
Factory I and II	107	2.6	1.6	0.2	8.4

TABLE 19 The means and standard deviations for six performance tests in five main groups of study

Variable	Factory I						Factory II			
	Exposed		Manual Controls		Office Controls		Exposed		Controls	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Adding test time (min)	19.1	6.2	19.6	6.2	14.7	5.1	21.8	9.7	19.0	7.8
errors (no.)	6.6	5.2	8.9	5.3	4.4	3.2	8.0	5.7	7.6	4.5
Tapping double plates										
60" - latches (no.)	129.5	17.0	134.6	13.8	133.9	17.5	147.2	17.2	144.6	14.6
- bridge hits (no.)	9.0	13.2	9.4	11.4	9.9	9.2	8.8	9.4	9.6	6.9
Tapping single plate										
60" - taps (no.)	348.5	41.5	345.3	34.2	357.6	28.1	361.4	40.1	370.2	42.4
Grip strength (kg)	63.0	9.2	60.1	9.3	58.1	9.0	61.3	10.5	63.2	9.6
Endurance (seconds)	39.7	16.3	37.9	16.7	30.7	14.5	27.2	8.7	24.1	9.0
One-hole test										
total No. of pins	290.1	37.7	289.7	41.1	294.1	36.2	295.9	43.8	291.7	29.2
Total time grasp (secs.)	61.8	16.6	57.9	13.4	60.7	22.2	48.1	16.9	56.2	16.1
Total time positioning (seconds)	92.0	13.7	95.6	13.1	88.6	16.5	94.7	11.9	95.5	15.3
Reaction time arm (m.secs)	119.1	22.5	136.6	33.0	127.2	26.9	134.3	31.3	133.7	41.1

Variable	Factory I			
	Exposed		Manual controls	
	Mean	SD	Mean	SD
Maximum slope arm (volts)	7.3	1.8	6.8	1.8
Frequency arm (Hz)	3.3	0.8	3.3	0.7
Reaction time leg (m.secs)	148.6	30.9	156.7	35.7
Maximum slope leg (V)	7.5	1.9	7.2	2.0
Frequency leg (Hz)	3.4	0.7	3.3	0.8
Reaction time visual (m.secs)	134.4	21.0	147.6	26.3
Maximum slope visual (V)	7.2	1.9	7.1	1.9
Frequency visual (Hz)	3.3	0.6	3.3	0.7

Factory II

Office Controls		Exposed		Controls	
Mean	SD	Mean	SD	Mean	SD
6.7	1.6	7.2	2.3	7.4	2.3
5.4	0.6	5.6	0.9	3.3	0.6
149.4	34.7	159.3	33.3	159.3	39.4
7.1	1.4	7.4	2.6	7.4	2.1
5.4	0.6	3.6	0.8	3.3	0.8
137.3	22.0	147.9	22.9	149.1	22.2
7.0	1.4	7.5	2.3	7.0	1.8
3.2	0.6	3.7	0.8	3.4	0.7

11.7.1. Associations between performance and biochemical tests

Associations were examined to see if meaningful, within exposed and control groups.

The association of each of the performance test with blood lead, lead in urine and amino-levulinic acid in urine was determined by calculating the correlation coefficient for exposed workers in Factory I and Factory II.

In Table 20 (Page 173) for the sake of clarity only correlations of $\pm$ 20 and over are shown.

The blood lead is correlated significantly and in the right direction (Appendix No. 2 for the expected sign of correlations), with one-hole test total position at 0.01 level in exposed workers Factory I and with frequency leg at 0.05 level in exposed workers Factory II. The other correlations tabulated are in the wrong directions, or not significant for the group's degree of freedom.

The urinary lead is correlated significantly and in the right direction with reaction time-maximum slope leg and maximum slope visual at 0.05 level and with grip strength in at 0.01 level in exposed Factory II.

The amino-levulinic acid in urine is correlated significantly and in right direction with tapping double plates 60" sec. number of bridge hits at 0.01 level in exposed group Factory I.

11.7.2. Associations between performance tests and population physical characteristics

The association of each performance test with age, weight, height and length of employment was determined by calculating the correlation

TABLE 20 The product moment correlation coefficients between biochemical and performance tests in the two exposed groups

Variable	Blood lead Factory I	Blood lead Factory II	Urinary lead Factory I	Urinary lead Factory II	ALA in urine Factory I	ALA in urine Factory II
Adding test: time				-.39*		
No.of errors						-.33
Tapping double plates 60"						
No.of latches				-.22		
No. of bridge hits					.32+**	.26
Tapping single plate 60"			.34**			
Grip strength				-.39**+		
Endurance				.28		
One-hole test total pins	.25*	.25		-.31		
total grasp				-.36*		
total positioning	.35+**			-.51**		
Reaction time arm						
Maximum slope arm		-.23		-.32		
Frequency arm		.28				.31
Reaction time leg			-.32**			
Maximum slope leg		-.21		r.35*+		
Frequency leg		.37+*				
Reaction time visual				.20		
Maximum slope visual		.26		-.35+*		
Frequency visual				-.32		

Legend

* significant at 0.05 level

** significant at 0.01 level

+ correlated in the right expected direction

coefficient within the four groups: Factory I exposed and controls and Factory II exposed and controls.

In Table 21 (pages 175 and 176) for the sake of clarity only correlations of ± 20 were tabulated.

The adding test - number of errors showed significantly correlations in the right directions (Appendix No. 21 for the expected sign of correlations), at 0.05 level with age in Factory I exposed. Tapping double 60 sec. number of latches showed significant correlation in the right direction with height at 0.05 level in Factory I controls. Tapping double 60 sec. number of bridge hits showed significant correlation, in right directions with weight at 0.05 level in controls Factory II.

Tapping single plate 60 sec. - number of taps showed significant correlations, in right directions with age at 0.05 level in Factory I exposed and with height at 0.05 level in Factory I controls. Grip strength showed significant correlations in right direction with age at 0.01 level in Factory I exposed and controls; with weight at 0.01 level in all four groups; with height at 0.01 level in Factory I exposed and controls, and at 0.05 level in Factory II controls, and with length of employment at 0.05 level in Factory I exposed.

One-hole test - total number of pins showed significant correlations in the right directions with age at 0.05 level and with height at 0.01 level in Factory II exposed.

One-hole test - total position showed significant correlations in right direction with age at 0.05 level in controls of both factories, with height at 0.05 level in Factory II exposed and with length of employment

TABLE 21 The product moment correlation coefficients between population physical characteristics and performance tests

Variable	Age				Weight				Height				Length of employment			
	FIe	FIIe	FIc	FIIc	FIe	FIIe	FIc	FIIc	FIe	FIIe	FIc	FIIc	FIe	FIIe	FIc	FIIc
Adding test time		-.24														
errors	.24+								-.26*							
Tapping double 60" No.of latches		-.20		.29	.24	.20	-.24				.26+	-.21				.42*
No.of bridge hits							.36**	-.37+		-.20		-.20	-.21			
Tapping single 60"	-.24+							.23	.22	-.23	.27+	-.24				
Grip strength	-.36+		-.29+	-.24	.58+	.66+	.37+	.44+	.54+		.38+	.58+	-.29+	.22	-.20	
Endurance																
One-hole test No.of pins		-.40+								-.47+		-.21				.24
Grasp						.28		.30	.30							-.46**
positioning		-.31	.23+	.35+						-.36+					.39+	
RT arm	.24+		.21+	.29+					-.20		-.23+	-.40+				.25

	Age				Weight			
	FIe	FIIe	FIc	FIIc	FIe	FIIe	FIc	FIIc
MS arm	-.30+**			-.37+**	.41+**	.48+**	.32+**	
Frequency arm					-.20	.30		
RT leg	.32+**	.28						
MS leg	-.35+**	-.29	-.26+**	-.40+*	.47+**	.46+**	.32+**	
Frequency leg					-.20	.30		
RT visual	.28+*	.48+*						
MS visual	-.28+*	-.24	-.20	-.35+**	.37+**	.42+*	.27+*	
Frequency visual								-.27

FIe - Factory I exposed
FIIe - Factory II exposed
FIc - Factory I controls
FIIc - Factory II controls

Legend: * - significant at 0.05 level
        **- significant at 0.01 level
        + - correlate in the right, expected direction

	Height				Length of employment		
FIe	FIIe	FIc	FIIc	FIe	FIIe	FIc	FIIc
.40+**		.26+*	.51+**		.22		-.35+*
			.22				
	.27		-.40+**				
.47**	-.25	.52+**	.52+**	-.22			-.26
	.50**			.32			-.38*
.39+**	-.21	.27+*	.24				-.25
				.25	.21*	.24	

at 0.01 level in Factory I controls. Reaction time arm showed significant correlations in the right direction with age at 0.05 level in Factory I exposed and controls and with height at 0.05 level in controls of both factories. The maximum slope arm showed significant correlations in right direction with age at 0.01 level in Factory I exposed and at 0.05 level in Factory II controls; with weight at 0.01 level in Factory I exposed and controls and in Factory II exposed; with height at 0.05 level in Factory I controls and at 0.01 level in Factory I exposed and Factory II controls; with length of employment at 0.05 level in Factory II controls. Reaction time leg showed significant correlations in right direction with age at 0.01 level in Factory I exposed and with height at 0.05 level in Factory II controls.

Maximum slope leg showed significant correlations in right direction with age at 0.05 level in controls both factories and at 0.01 level in Factory I exposed; with weight at 0.01 level in Factory I exposed and controls and Factory II exposed; with height at 0.01 level in Factory I exposed and controls and Factory II controls.

Reaction time visual showed significant correlation in right direction with age at 0.05 level in Factory I exposed and at 0.01 level in Factory II exposed.

Maximum slope visual showed significant correlations in right direction with age at 0.05 level in Factory I exposed and Factory II controls; with weight at 0.05 level in Factory I controls and Factory II exposed and at 0.01 level in Factory I exposed; with height at 0.05 level in Factory I controls and at 0.01 level in Factory I exposed.

In conclusion the performance tests - one hole test number of pins, reaction time arm, leg and visual showed consistent and statistically significant correlations with age while grip strength, maximum slope leg and visual showed constant and statistically significant correlation with age and weight; maximum slope arm showed correlation with age, weight and height.

The association of tests with length of employment showed a rather confused picture and as the variable is likely to be associated with age it is considered later in combination with age and in the exposed group only.

11.7.3. Analysis of variance

Comparisons between exposed workers and controls in Factory I and Factory II

Intercorrelations between population physical characteristics group variables and biochemistry group variables on the one hand and performance tests group variables on the other hand were examined to see if there was a need to adjust the performance group variables for their dependence on the first two groups of variables before comparing means.

The performance variables which showed no significant association with any of the populations physical variables and biochemical variables were adding   test-time to perform, adding test number of errors, tapping double plates 60 sec. trial-number of latches and bridge hits, tapping single plate 60 sec. trial, number of taps, one hole time of total position, and grasp, endurance, frequency arm, frequency leg and frequency visual.

A simple analysis of variance was therefore carried out on all
of these variables, except endurance, to test if the overall difference
between the means of the five groups was statistically significant.
For endurance it was shown that there was likely to be a difference in
the results between Factory I and Factory II because of the observer
error, therefore for this variable two separate analysis of variance
were made, one to compare exposed workers, manual and office controls
in the Factory I and another to compare exposed workers and controls in
Factory II.

The results of the F test are shown in Table 22:

TABLE 22 Analysis of Variance, comparisons between means of
five groups: Factory I exposed, office and manual controls,
Factory II - exposed and controls

Variable	F	p = statistically significant
Adding test		
time to perform	5.763	0.001
No. of errors	5.261	0.001
Tapping double plates 6" No. of latches	3.411	0.001
Tapping single plate 60" No. of taps	2.499	0.043
One-hole test total time grasp	3.134	0.016

Statistically significant differences were found for variables:
adding test-time to perform, adding test-number of errors, tapping
single plate 60 sec. trial - number of taps, tapping double plates

60 sec. trial - number of latches, one hole-time of total grasp and for endurance in Factory I but not in Factory II. For these variables separate comparisons between pairs of means were made using the "T" test. The results are shown in Tables Nos. 23, 24, 25, 26, 27. (Pages 181, 182, 183,184 and 185). For the variables where F test showed no statistically significant difference overall betwe n the means the data was examined to see if there was any evidence of meaningful difference between exposed and control workers in Factory I or in Factory II separately that could have been concealed in the overall comparison of the five groups; but differences between exposed and control workers were not consistent in the two factories and no further statistical tests were carried out.

11.7.4. <u>Analysis of Covariance</u>

Examination of the simple correlation coefficients showed that the scores on the one-hole test (total number of pins in seven trials) showed a negative association with age, while reaction time arm, reaction time leg and reaction time visual showed positive association with age.

Grip strength, maximum slope leg, and maximum slope visual were all negatively associated with age and positively associated with weight.

Maximum slope arm showed a similar association with age and weight and also a positive association with height. Therefore, before making comparisons between the various groups of workers it was necessary to adjust the test scores for age, to allow for the differences between the groups in these factors where they were relevant.

TABLE 23 Adding test- time to perform, comparison between pairs of means

Comparisons	Difference between means	SE of difference	t	Significance level
Factory I exposed versus Factory I manual controls	-.05	1.5	-0.3311	N.S.
Factory I exposed versus Factory I office controls	4.4	1.3	3.4029	P< 0.001
Factory I manual controls versus Factory I office controls	5.0	1.6	3.144	P< 0.01
Factory II exposed versus Factory II controls	2.8	1.8	1.5681	N.S.
Factory I exposed versus Factory II exposed	-2.7	1.5	-1.7883	N.S.
Factory I manual controls versus Factory II controls	0.6	1.8	0.3360	N.S.

TABLE 24 Adding test - number of errors, comparison between pairs of means

Comparisons	Difference between means	SE of difference	t	Significance level
Factory I exposed versus Factory I manual controls	-2.3	1.1	-2.1798	P < 0.05
Factory I exposed versus Factory I office controls	2.2	0.9	2.4365	P < 0.02
Factory I manual controls versus Factory I office controls	4.5	1.1	4.0405	P < 0.001
Factory II exposed versus Factory II controls	0.4	1.3	0.3198	N.S.
Factory I exposed versus Factory II exposed	-1.4	1.1	-1.3268	N.S.
Factory I manual controls versus Factory II controls	1.3	1.3	1.0395	N.S.

TABLE 25 Tapping single plate 60" - number of taps, comparison between pairs of means

Comparisons	Difference between means	SE of difference	t	Significance level
Factory I exposed versus Factory I manual controls	3.2	8.5	0.3875	N.S.
Factory I exposed versus Factory I office controls	-9.1	7.1	-1.2878	N.S.
Factory I manual controls versus Factory I office controls	-12.3	8.7	-1.4112	N.S.
Factory II exposed versus Factory II controls	-8.8	9.7	-0.906	N.S.
Factory I exposed versus Factory II exposed	-12.9	8.3	-1.5623	N.S.
Factory I manual controls versus Factory II controls	-24.9	9.7	-2.5654	P < 0.02

TABLE 26 Tapping double plates 60" - number of latches, comparison between pairs of means

Comparisons	Difference between means	SE of difference	t	Significance level
Factory I exposed versus Factory I manual controls	-5.1	3.6	-1.4163	N.S.
Factory I exposed versus Factory I office controls	-4.4	3.1	-1.4278	N.S.
Factory I manual controls versus Factory I office controls	0.7	3.8	0.1841	N.S.
Factory II exposed versus Factory II controls	2.6	4.2	0.6142	N.S.
Factory I exposed versus Factory II exposed	-17.7	3.6	-4.9155	P < 0.001
Factory I manual controls versus Factory II controls	-10.0	4.2	-2.3626	P < 0.02

TABLE 27 One hole test - total grasp, comparison between pairs of means

Comparisons	Difference between means	SE of difference	t	Significance level
Factory I exposed versus Factory I manual controls	3.9	4.5	0.8698	N.S.
Factory I exposed versus Factory I office controls	1.1	4.0	0.2743	N.S.
Factory I manual controls versus Factory I office controls	-2.8	4.6	-0.6031	N.S.
Factory II exposed versus Factory II controls	-8.1	4.6	-1.7756	N.S.
Factory I exposed versus Factory II exposed	13.7	4.2	3.2700	P <0.01
Factory I manual controls versus Factory II controls	1.7	4.8	0.3517	N.S.

The amount of adjustment is determined by the regression of the test scores on the associated variables, the adjusted mean in each group being calculated by the following formulae:

To adjust a test score for age only

Adjusted mean = observed mean − $b(\bar{x}_1 - \bar{\bar{x}}_1)$

where b = simple regression coefficient of test score on age obtained by pooling the data from all the groups being compared (it measures the average change in test score for an increase of one year of age)

$\bar{x}_1$ = mean age of specific group

$\bar{\bar{x}}_1$ = mean age of combined groups.

For a specific group this formula gives the mean test score that would be expected if the mean age of the group had been the same as that of all groups combined.

To adjust a test score for age, height and weight multiple regression is required using the following formula:

Adjusted mean = observed mean − $b_1(\bar{x}_1 - \bar{\bar{x}}_1) - b_2(\bar{x}_2 - \bar{\bar{x}}_2) - b_3(\bar{x}_3 - \bar{\bar{x}}_3)$

where $b_1 (i=1,2,3)$ denotes the partial regression coefficients of test score on age, on height and on weight respectively e.g. the partial regression of a test score an age shows the average change in the test score for an increase of one year of age assuming that height and weight are held constant.

$\bar{x}_1$ = mean age of specific group

$\bar{x}_2$ = mean height of group

$\bar{x}_3$ = mean weight of group

$\bar{\bar{x}}_1$, $\bar{\bar{x}}_1$ and $\bar{\bar{x}}_3$ = mean age, height and weight respectively of all groups combined.

The amount of adjustment is determined by the regression of the test scores on the associated variables, the adjusted mean in each group being calculated by the following formulae:

To adjust a test score for age only

Adjusted mean = observed mean $- b(\bar{x}_1 - \bar{\bar{x}}_1)$

where b = simple regression coefficient of test score on age obtained
by pooling the data from all the groups being compared (it measures the average change in test score for an increase of one year of age)

$\bar{x}_1$ = mean age of specific group

$\bar{\bar{x}}_1$ = mean age of combined groups.

For a specific group this formula gives the mean test score that would be expected if the mean age of the group had been the same as that of all groups combined.

To adjust a test score for age, height and weight multiple regression is required using the following formula:

Adjusted mean = observed mean $- b_1 (\bar{x}_1 - \bar{\bar{x}}_1) - b_2(\bar{x}_2 - \bar{\bar{x}}_2) - b_3(\bar{x}_3 - \bar{\bar{x}}_3)$

where $b_1(i=1,2,3)$ denotes the partial regression coefficients of test score on age, on height and on weight respectively e.g. the partial regression of a test score an age shows the average change in the test score for an increase of one year of age assuming that height and weight are held constant.

$\bar{x}_1$= mean age of specific group

$\bar{x}_2$= mean height of group

$\bar{x}_3$= mean weight of group

$\bar{\bar{x}}_1$, $\bar{\bar{x}}_2$ and $\bar{\bar{x}}_3$ = mean age, height and weight respectively of all groups combined.

Table 29 shows the regression coefficients derived from pooled calculations for the 5 main study groups, together with their significance level.

TABLE 29 Simple and partial regression coefficients of performance tests on age, weight and height

Performance test	Regression coefficients		
	Age (years	Weight (kg)	Height (cm)
One hole test total pins	-0.675 (P< 0.02)		
Reaction time arm	0.736 (P <0.01)		
Reaction time leg	0.508 (P <0.05)		
" "visual	0.479 (P< 0.01		
Grip strength*	-0.215 (P=0.001	0.468 (P=0.001)	
Max.slope leg*	-0.531 (P=0.001)	0.562 (P=0.001)	
" visual*	-0.392 (P <0.01)	0.513 (P=0.001)	
" arm*	-0.372 (P=0.01)	0.571 (P=0.001)	0.434 (P=0.05)

legend: * partial regression coefficients are shown for these tests

Table 30 (Page 188) shows the adjusted means which were then compared by an analysis of covariance.

The overall F test showed statistically significant difference between the five groups for reaction time arm (p=0.05), reaction time visual (P< 0.01) and grip strength (P< 0.01).

TABLE 30 Adjusted and unadjusted means of performance tests in five study groups:- Factory I - exposed, office and manual controls, Factory II exposed & controls

Performance tests

Groups of subjects	One hole No.of pins Unadj. M	Adj. M	RT arm Unadj. M	Adj. M	RT leg Unadj. M	Adj. M	RT visual Unadj. M	Adj. M	Grip strgth Unadj. M	Adj. M	MS leg Unadj. M	Adj. M	MS vis Unadj. M	Adj. M	MS arm Unadj. M	Adj. M
Factory I exposed	290.1	289.7	119.1	119.6	148.6.	148.8	134.5	134.8	62.7	62.1	7.5	7.3	7.2	7.0	7.3	7.1
Factory I manual controls	289.7	289.7	136.6	137.0	156.7	157.0	147.7	147.9	60.2	60.8	7.2	7.2	7.1	7.1	6.8	6.9
Factory I office controls	294.1	292.6	127.2	128.6	149.4	150.4	137.4	138.2	57.7	57.6	7.1	7.0	7.0	6.9	6.7	6.5
Factory II exposed	295.9	298.6	134.3	132.1	159.3	158.6	148.0	146.8	61.3	61.5	7.4	7.6	7.5	7.7	7.2	7.4
Factory II controls	291.7	293.4	133.7	131.8	159.3	158.1	149.2	148.2	63.2	63.8	7.4	7.6	7.6	7.7	7.4	7.7
F	0.31		2.38		0.74		3.38		3.36		0.98		1.81		1.82	
Significance level	$P > 0.05$ nonsig.		$P = 0.05$		$P > 0.05$ nonsig.		$P < 0.01$		$P < 0.01$		$P > 0.05$ nonsig.		$P > 0.05$ nonsig.		$P > 0.05$ nonsig	

For these three tests comparisons were made between pairs of means where the difference would be considered of interest, and the differences tested for statistically significance. The results are shown in Table 31 (Page 190). Since it was thought that in the exposed groups of workers the results of the psychomotor tests might be influenced by length of employment the relationship between tests and length of employment was examined in the two exposed groups. Since length of employment was related to age the partial regression coefficient of each test on length of employment with age held constant was calculated from the pooled data of the two groups.

In the Factory II exposed group none of the partial regression coefficient was statistically significant.

In the Factory 1 exposed group the partial regression coefficient was statistically significant for the tests tapping single 60 sec., reaction time arm, reaction time visual - Table 28:-

TABLE 28 Partial regression coefficients of performance tests on age, and on length of employment for exposed workers in Factory I

	Partial Regression Coefficients	
Performance	Regression on age with length of employment held constant	Regression on length of employment with age held constant
Tapping single plate 60" - No. of taps	-3.08 (P=0.001)	3.04 (P=0.005)
Reaction time arm	1.311 (P=0.006)	-1.13 (P=0.048)
Reaction time visual	1.239 (P=0.001)	-1.26 (P=0.006)

Since the results were not consistent in the two factories and

TABLE 31 Comparisons between pairs of adjusted means for reaction time arm, reaction time visual and grip strength

| | Performance tets | | | | | | | | |
| | Reaction time arm | | | Reaction time visual | | | Grip strength | | |
Comparison	Difference between adjusted means	t	Significance level	Difference between adjusted means	t	Significance level	Difference between adjusted means	t	Significance level
FI E vs MC	-17.4	-2.74	P< 0.01	-13.1	-2.68	P< 0.01	1.3	0.78	N.S.
FI E vs OC	-9.0	-1.67	N.S.	-3.4	-0.80	N.S.	4.5	3.21	P< 0.01
FI MC vs OC	-8.4	1.19	N.S.	9.7	1.87	N.S.	3.2	1.72	N.S.
FII E vs C	-0.3	0.04	N.S.	-1.4	-0.24	N.S.	-2.3	-1.16	N.S.
FI E vs FII E	-12.5	-1.96	P=0.05	-12.0	-2.44	P< 0.02	0.6	0.28	N.S.
FI MC vs FII C	5.2	0.67	N.S.	-0.3	-0.05	N.S.	-3.1	1.52	N.S.

Legend: F I E = Factory I exposed

FI MC = Factory I manual controls

FI OC = Factory I office controls

F II E = Factory II exposed

F II C = Factory II controls

association of these tests with length of employment when age was held constant showed the opposite result to that expected no analysis for means adjusted for length of employment was made.

11.7.5. Summary on results for each of performance tests.

Adding test

(a) Time to perform

Table 19 showed that in Factory 1 the mean of time to perform (minutes) was shorter for controls office workers than for manual controls.   There was no difference between exposed and manual controls, so indicating that the exposed were not at disadvantage in this case. However in Factory 11 a difference in mean value between exposed and controls appeared in that the exposed perf   ed poorer than controls.

An alaysis of variance for 5 groups (Table 22) (Page 179) F = significant, $p < 0.001$. Comparisons between pairs of mean ("t" test) gave a significant difference ($P < 0.001$) between factory I exposed versus Factory I office controls i.e. the exposed performed poorer than office controls;   this was expected as a result of different intellectual level between two groups.   The comparison between pair of means gave also a $P < 0.01$ between manual controls Factory 1 and office controls Factory 1;   this result was expected to appear as a result of different intellectual level between two groups and proved correct the idea to divide the controls in Factory 1 in office and manual - not only for differences in physical work they perform but for differences in their intellectual level.

(b) Number of errors

Table 19 shows that in Factory I the means indicate that the control office workers made less number of errors than manual controls or exposed

workers.   Also in terms of means of errors the exposed performed poorer than manual controls.   An analysis of variance of five groups gave F = significant (P 0..01) (Table 22).   Comparisons between pairs of means ("t" test) showed:

Factory I exposed versus Factory I manual controls P < 0.05

Factory I exposed versus Factory I office controls P < 0.02

Factory I manual controls versus Factory I office controls P < 0.001

No statistically significant differences could be found in Factory II.

From the above results of adding test it can be seen that all the significant findings were expected as a result in dividing the subjects in the five groups.   Unless positive findings in majority of other performance tests could be found in Factory I is no reason for judging the significant findings of the adding test related to lead.   It is interesting to note the findings of Repko et al (1975) on a similar test. On arithmetic computation test they reported that on average the lead group of subjects performed better than controls and only those people with blood lead above 100µg/100ml. blood performed poorer than controls.

Tapping Test

(a)   Tapping double plates 60 sec. - number of latches

The mean number of latches in Factory I is poorer for exposed than controls (Table 19) (Page 170).   No big difference in mean values between manual and office controls was found.

In Factory II a small difference in mean showed that exposed performed better than controls.

Analysis of variance between five groups which showsthat at least one group could differ from the others gave a F significant, P < 0.001.

Comparisons between pairs of means ("t" test) (Table 26) (Page 184) showed that: Factory I exposed performed poorer than Factory II exposed ($P < 0.001$) and Factory I manual controls performed poorer than Factory II controls ($P < 0.02$). The significant differences found between factories were not expected and since the condition of experiment was similar in both factories no other explanation than motivation could be given for these findings.

The lack of significant findings within factories indicate that this is the most likely explanation.

(b) Number of bridge hits

Table 19 (Page 170) shows that in Factory 1 practically no difference in mean number of bridge hits could be found among the three groups. In Factory II a small difference appeared, the mean bridge hits indicate that the exposed performed better than controls.

Analysis of variance for the five groups (Table 22) (Page 179) show F = nonsignificant, therefore no comparisons between pair of means ("t") were necessary.

(c) Tapping single plate 60 sec. number of taps

The mean number of taps shown in table 19 is bigger in office controls in Factory 1 than that of exposed and manual controls. No noticeable difference between exposed and manual controls could be found.

Factory II controls show a bigger number of mean taps, therefore they performed better than exposed.

Analysis of variance between five groups (Table 22) (Page 179) showed F = significant, $P < 0.043$. Comparisons between pairs of means ("t") showed that Factory II controls performed better than Factory I controls ($P < 0.02$).

This was an unexpected findings and this is consistent with differences between factories controls for number of latches. Again motiviation for Factory II controls to perform better could be given as an explanation for this finding.

One hole test

(a) Total number of pins

The mean number of pins (Table 19) (Page 170) indicate that Factory I office controls performed slightly better than manual controls or than exposed. The exposed, poorer performers than office controls show means slightly better than manual controls.

In Factory II the same table shows that the exposed performed better than controls.

Analysis of covariance (Table 30) (Page 18?) in five groups for adjusted and unadjusted means gave a $P > 0.05$=nonsignificant.

No comparisons between pairs of means were necessary.

(b) Grasp-total time

In Table 19 (Page 170) the means in Factory I indicate that manual controls performed better than office controls or exposed. The office performed better than exposed.

In Factory II the means show that the exposed performed better than controls.

Analysis of variance for the five groups (Table 22) (Page 179) gave a F = significant $P < 0.016$. Comparisons between pairs of means showed that Factory I exposed performed better than Factory II exposed (Table 27) (Page 185).

(c) Position-total time

For means of position the situation is similar to total number

of pins in Factory I.   In Factory II the means show the same tendency
as for number of pins and grasp, i.e. the exposed performed better than
controls.   Analysis of variance for the five groups showed F = non-
significant so that no comparisons between pairs of means were necessary.

The conclusion which can be drawn is that the differences in grasp
between Factories were not expected and again a motivation from Factory
1 exposedgroup could be the cause.

In analysing the tendency of means, even they did not come to be
significant,it showed the same direction for the three variables,
i.e. the exposed better than controls in Factory II.   This is similar to
Repko et al (1974) findings for the eye-hand co-ordination test they
had used;   they reported that the controls showed not only significant
slower response time but also a significantly greater amount of
variability in their performance.

Reaction time arm

In table 19 (Page 170) the mean reaction time for workers in
Factory I showed that exposed workers were quicker than the controls,
in their reaction to an electrical stimulus.   Between the two groups of
controls the means showed that office workers were better than manual
controls.

In Factory II no noticeable difference between means of two groups
appeared.   Analysis of variance for the five groups showed an F = limit
of significance, $P=0.05$.   Comparisons between pairs of means ("t") showed
that Factory I exposed reacted more quickly than Factory I manual controls
($P < 0.01$).

(a)   Maximum slope arm

In Table 19 the mean slope for Factory I groups showed that the mean
maximum slope for exposed is bigger than that of manual controls,

therefore the exposed performed better.

In Factory II the difference in mean between exposed and controls is very small so that at the analysis of covariance for the five groups (Table 30) (Page 188) with adjusted and unadjusted means the results come nonsignificant ($P > 0.05$).

(b) Frequency

In table 19 (Page 170) the means of frequency of workers performing reaction time was around 3.3 Hz. in between and within the factories groups. Analysis of variance between the five groups showed F = nonsignificant.

The important findings from the three variable of this test (reaction time, maximum slope and frequency) is that of tendency of exposed to perform better than controls in Factory I and no differences between groups in Factory II. From these results the hypothesis of decrement in performance resulted from lead poisoning is excluded at this level of blood lead. On the contrary, the exposed are better in Factory I than controls; this is similar finding with results from a reaction time study performed before in Factory II (Milburn 1973, Milburn, Litran and Crockford 1976) and is concordant with Repko et al (1974) results in which their lead workers performed better than controls for some of the performance tests they used in their battery of tests.

The frequency of hand grip response was selected because it was considered to be free of motivational attitude which may affect other performance tests. The frequency should be independent of grip strength as it is a measure at which the total grip strength start. Experiments on the right and left hand of two male subjects and one woman subject in the

Institute of Occupational Health, showed that the frequency of response
did not depend on strength and that the results were very consistent.
That is in a remarkable agreement with the frequency found in the
present study which indicates by their nonsignificant differences between
factories and within factories that the neuromuscule system has not been
adversely affected by lead.

Reaction time leg

The mean reaction time leg for workers (Table 19) (Page 170) in
Factory I showed that the exposed workers were quicker in their reaction
to an electrical stimulus to the leg than the controls.   The biggest
difference came to be in means between exposed and manual controls i.e.
the exposed performed better than controls.

In Factory II the means of reaction time leg came to be equal
between exposed and controls.

At an analysis of variance between the five groups the difference
observed in Factory I did not come significant so that F = nonsignificant,
$P > 0.05$.   No comparisons between pairs of means were necessary.

(a)   Maximum slope leg

From Table 19 the mean maximum slope in Factory I workers was
bigger in exposed than in controls, the biggest difference being between
office controls and exposed.

In Factory II the mean maximum slope leg was the same in exposed
and controls.   Analysis of variance between five groups showed F =
nonsignificant, $P > 0.05$.

(b)   Frequency leg

The mean frequency (Table 19) for leg of workers in Factory I and

in Factory II groups were around 3.3 Hz. No significant difference has been found at the analysis of variance, F =nonsignificant, P > 0.05.

The important findings of this test are the similarity in the results with reaction time arm. Again the two important findings, better performance by the lead exposed workers than controls, and the consistent frequency means in all groups sustain the point of the lead exposed group not being affected by lead in their performance.

Reaction time visual

The mean reaction time to a visual stimulus in workers (Table 19) (Page 170) of Factory I showed that the exposed performed quicker than controls; the biggest difference appeared between exposed and manual controls. In Factory II this tendency in means is again found but the differences between two groups, exposed and controls, is very small.

Analysis of variance for the five groups showed significant differences, F = significant, P < 0.01. Comparisons between pairs of means ("t") showed that Factory I exposed performed better than Factory I manual controls P < 0.01, and that Factory I exposed performed better than Factory II exposed, P < 0.02.

(a) Maximum slope visual

In table 19 the mean maximum slope for reaction time to a visual stimulus in Factory I showed that the exposed were better than controls; the biggest difference appeared between exposed and office controls. In Factory II the controls seem to have better means values than exposed. Analysis of covariance for adjusted and unadjusted means in the five groups was nonsignificant, P > 0.05.

(b) Frequency visual

In Table 19 the mean frequency of workers performing reaction time visual was 3.2-3.4 Hz. in all groups with the exception of Factory II exposed where it was 3.7 Hz.; however at the analysis of variance on the five groups no statistically significant differences were found.

The important finding for this test is the similarity in results with reaction time arm and leg, in that the exposed performed better than controls and the consistent frequency means values for all groups. Such constant findings for the three reaction times tests give the possibility of concluding that the performance is not affected by lead at this level of absorption.

An unexpected finding was the significant difference between Factory I exposed versus Factory II exposed in which the Factory I exposed group performed better. Here again, only an unknown motivational factor could be involved in explaining this difference.

Grip Strength

The mean grip strength values expressed in kg. are shown in Table 19 for the five groups of workers. The mean value is bigger in Factory I exposed than the controls i.e. they performed better than controls; the biggest difference is between exposed and office controls. In Factory II this situation is changed, so that the mean values show that controls are slightly better than exposed.

Analysis of covariance between five groups with adjusted and unadjusted means showed significant differences, $P < 0.01$. Comparisons between pairs adjusted means showed that Factory I exposed performed better than Factory I office controls, $P < 0.01$. No significant differences

appeared between Factory II groups.

The above difference found was expected in view of heavy manual work the exposed performed, in comparison to office workers.

The nonsignificant difference between exposed and manual controls in both factories showed that these four groups have been correctly matched in view of the amount of physical effort they perform for their work. The lack of findings showed that the exposed populations are not affected by lead at the present level of absorption.

Repko et al (1974) showed in their exposed workers that grip strength was better than that of the controls, and they hypothetised that exposed workers felt that it was necessary for them not to show their suspected weakness, and exerted greater forces on the strength pulls; this hypothesis was supported by the finding of an inverse relationship between muscular strength and endurance.

Endurance

The mean values of endurance, expressed in seconds, for the workers tested are shown in Table 19. In Factory I the exposed performed better than controls; the biggest difference appeared between exposed and office controls.

In Factory II the findings are similar, the exposed performed better than controls.

Because for this test there was a possibility of a difference in results between factories due to the observer error, two separate analysis of variance were performed, one for Factory I groups and another for Factory II groups.

Analysis of variance between the three Factory I groups revealed statistically significant differences $P < 0.01$. Comparisons between pairs

of means showed significant differences between exposed who performed
better than office controls P < 0.01.

Analysis of variance between Factory II groups showed no
statistical difference.

Important findings are that even the analysis of variance did
not show, a tendency in mean values indicate that controls manual
are poorer performers than exposed. This is positively correlated to
grip strength findings and does not indicate a decrement in lead exposed
workers at the present level of lead absorption.

Repko et al (1974) reported that in terms of muscular endurance
their controls were better than exposed (P < 0.01); also no significant
differences were found among blood lead subgroups, there was a large
decrease in endurance at blood lead level 60-69 ug/100 ml.

The authors' explanation was that people of higher blood lead
subgroups exerted themselves to greater extent on strength pulls than
people of lower blood lead subgroups and therefore were unable to
maintain their endurance for as long as lower subgroups.

11.7.6. Tremor tests

The tremor tests have been performed on subjects from Factory I
only. The equipment for tremors had been borrowed from the Royal
Naval Environmental Medicine Unit.

The four tremors analysed were: intention, postural, balance
board - eyes open and eyes shut. In the chapter of methods (10.8)
details on procedure were given. The sampling time for each tremor was
ten times of two seconds.

The mean of square amplitude of power for each variable over a
spectrum of frequency of 0.5-0.32 Hz. for the three groups of subjects,
exposed, manual controls and office controls, had been analysed by
computer and the results are given in Figures 41-44 (Pages 203, 204,
205 and 206).

The total number of subjects tested for all four tremors was 98,
from whom 46 exposed to lead, 22 manual controls and 30   office controls.

The intention tremor seem to be the most sensitive among the four
tremors tested. In figure 41 the mean power of intention tremor, for
the three groups has been plotted. The line from 0- 2 Hz. represents
the movement of the whole body due to heart beats or to visual correction.
The physiological tremor should be judged between 6-12 Hz. interval
(Lippold,1971). As can be seen over the 8-12 Hz. spectrum small differences,
nonsignificantly statistic, appeared. The picture of the exposed group
is similar to that of manual controls, excluding lead as an etiological
factor for the small differences. The explanation for this difference
could be in other factors, which usually influence tremor, such as age,
emotional strain, visual acuity, fatigue etc.

Postural tremor plotted in figure 42 show some differences,
statistically significant ($P < 0.01$) between manual controls group, who
appear with a bigger amount of tremor and the exposed group. An
explanation for this finding could be the difference in body weight or
the amount of physical work the subjects had done prior to be tested.
Figures 43-44 show the plotted tremor on balance board with eyes open
(Fig.43) and eyes shut (Fig.44). If people tested should have presented
more tremor for balance board eyes shut, the more sensitive of these

Figure 41 – The mean square amplitude of power of intention tremor
for exposed, manual and office controls (Factory I)

Legend: ✷ exposed to lead
         ◆ office controls
         ◇ manual controls
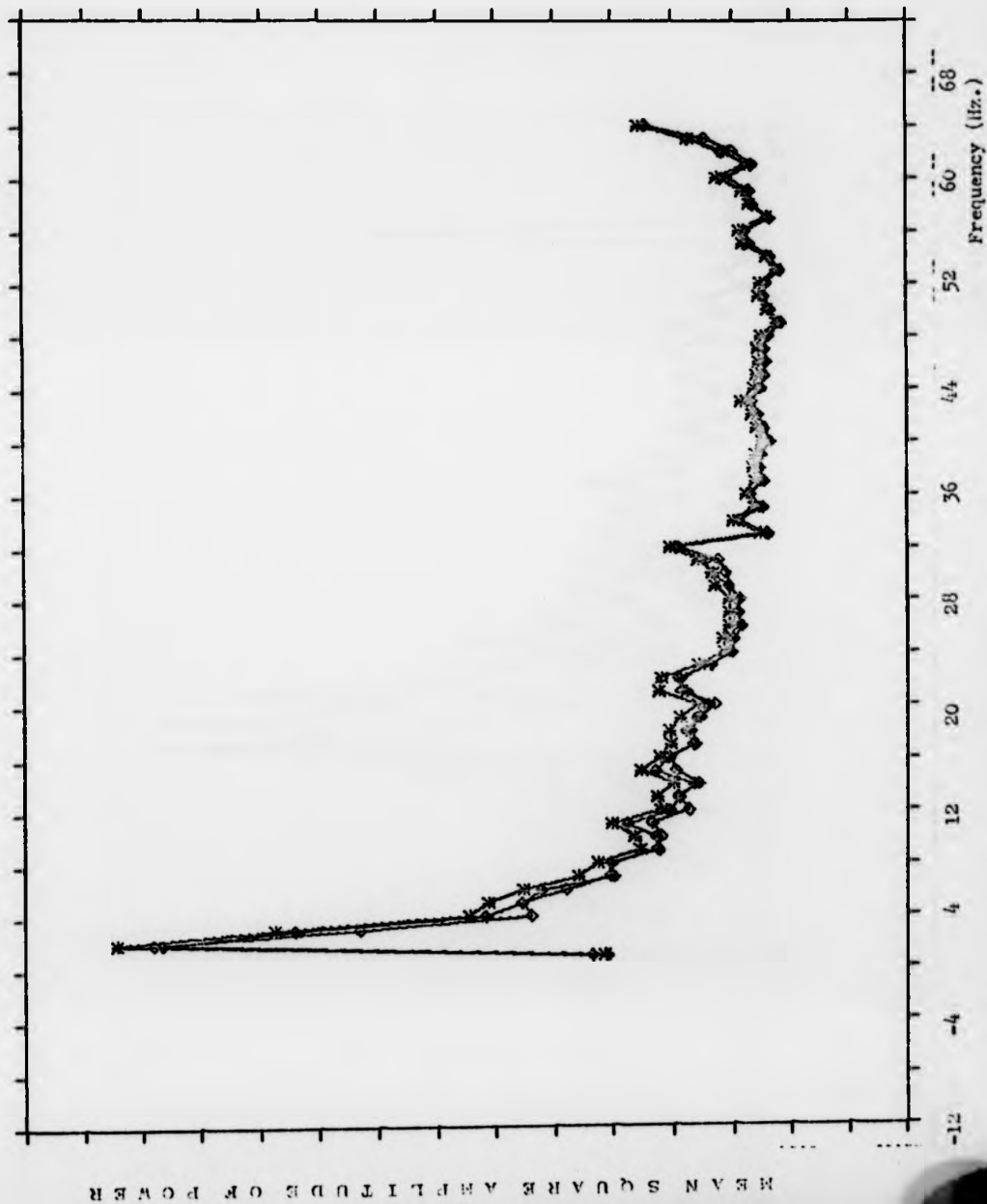
Figure 42 - The Mean Square Amplitude of power of postural tremor for exposed, manual and office controls (Factory 1)

Legend: ¥ exposed to lead
◆ office controls
◇ manual controls
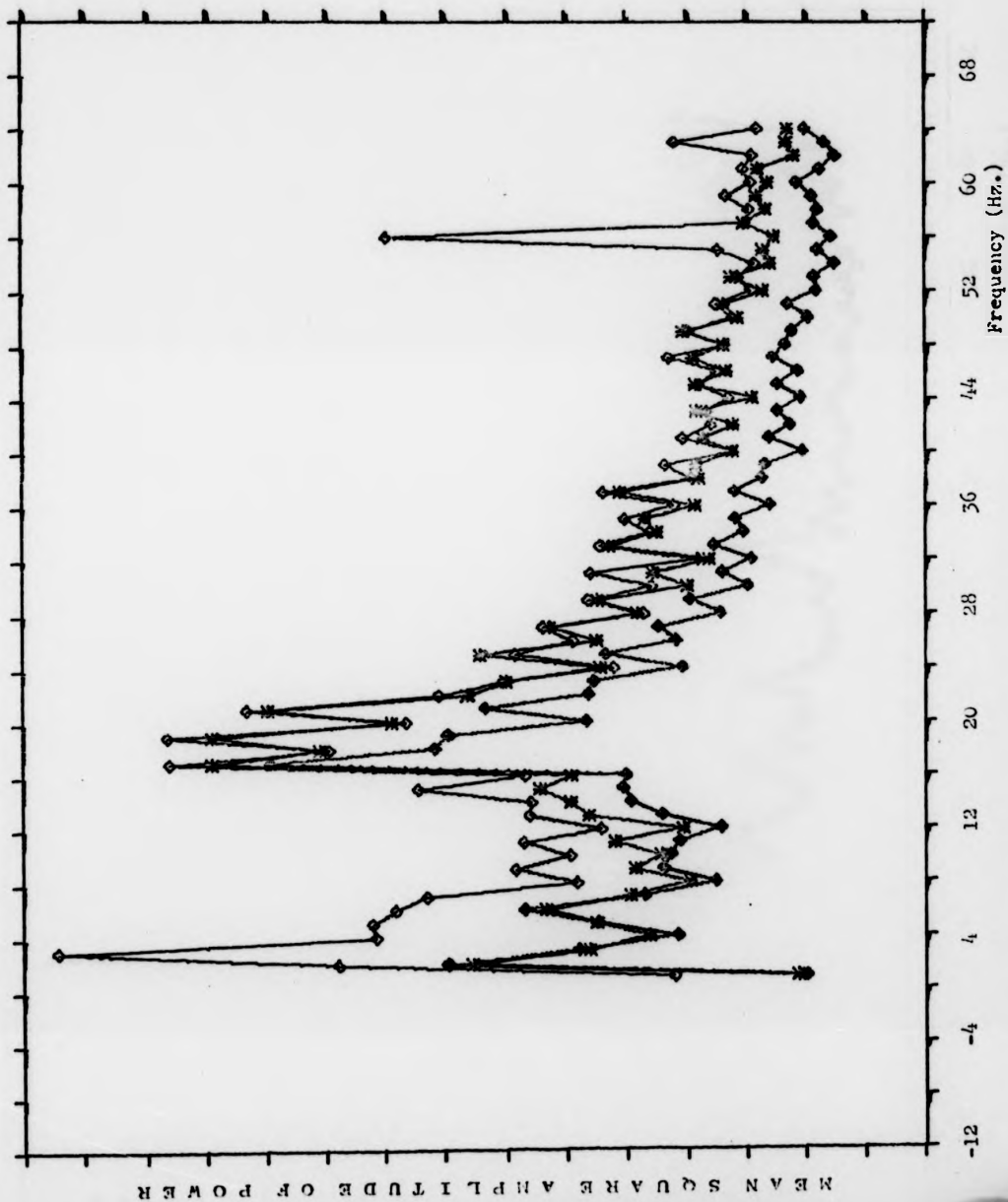
Figure 43 - The mean square amplitude of power of balance board tremor
eyes open for exposed, manual and office controls (Factory 1)

Legend: ✛ exposed to lead
◆ office controls
◇ manual controls
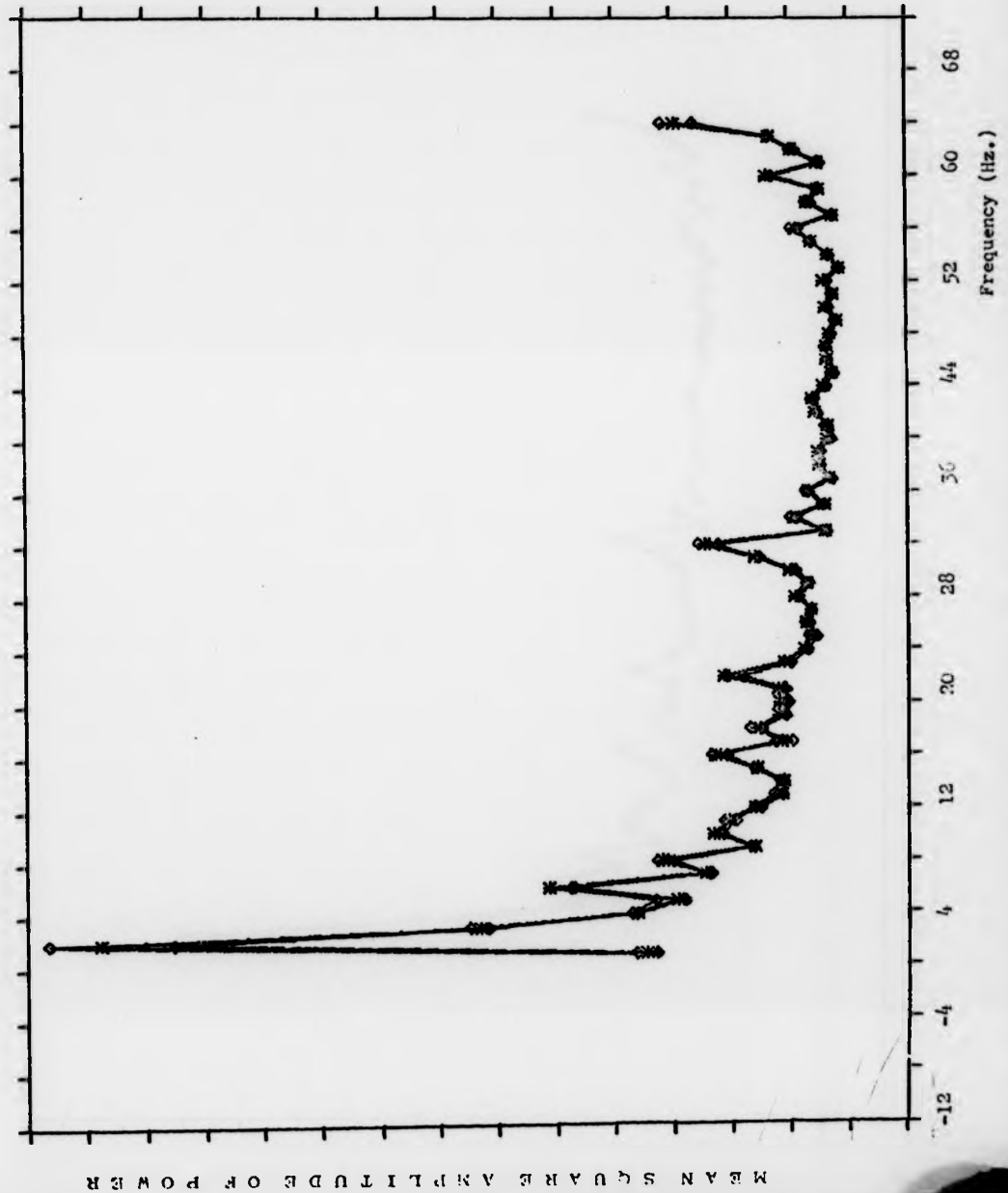
Figure 44 - The mean square amplitude of power of balance board tremor
eyes shut for exposed, manual and office controls (Factory I)

Legend: exposed to lead
office controls
manual controls
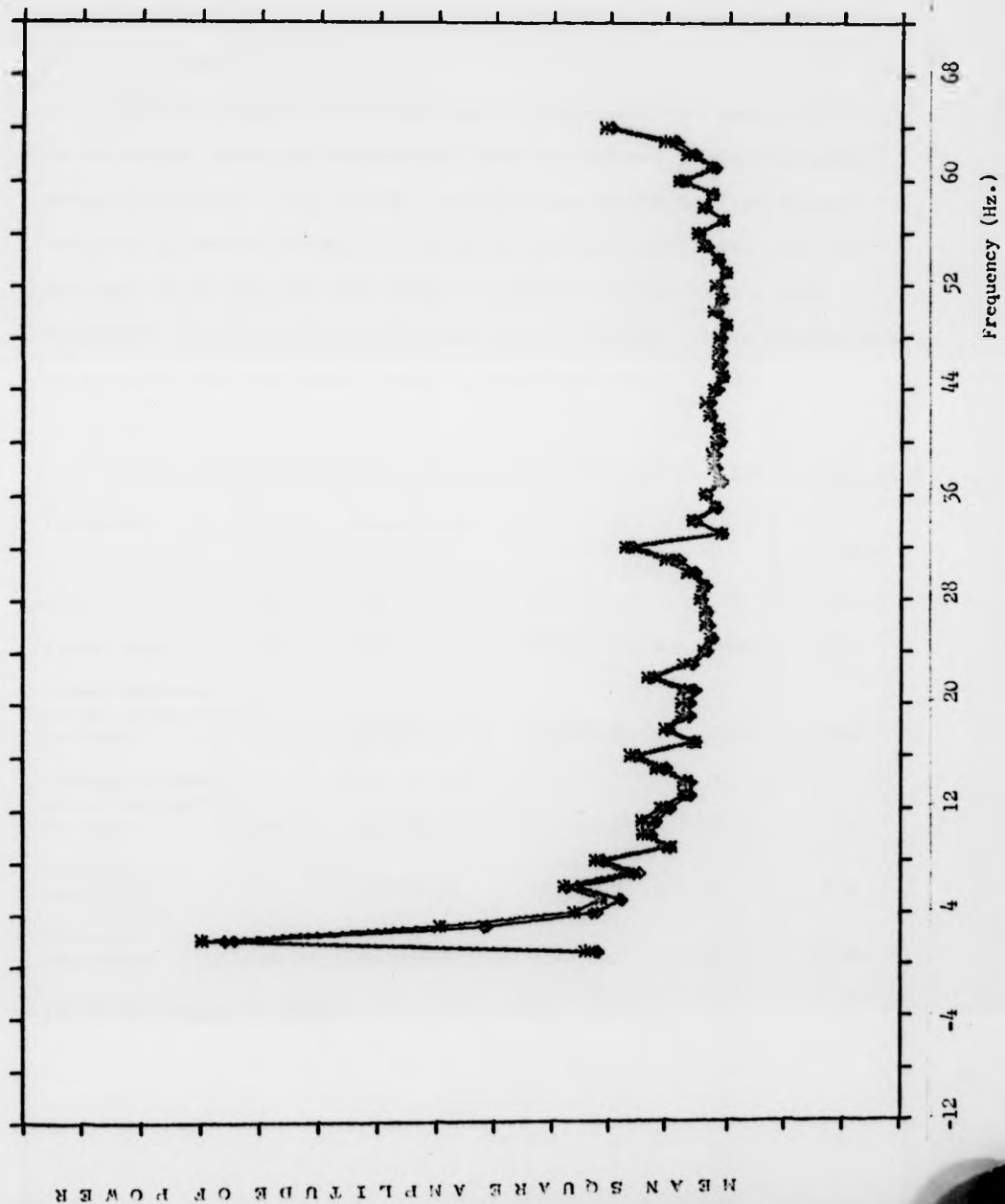
two tremors, lead should have been taken into consideration as a possible etiological factor. As can be seen from Figures 43-44, no significant differences appeared for both these tremors.

11.8 Nerve Conduction velocity

In the chapter of methodology, section 10.1 the reason of choosing the group of exposed and controls workers for the present study in Factory I was shown; for the same reason the individual results for nerve conduction velocity were not available; only the results concerning the two groups - exposed and controls - were available from Archibald's Progress Report (1976). These results are reproduced from the above report in Table No. 32:

TABLE 32 The paired "t" test of exposed and controls in Factory I

Parameter	Nr.	Mean + SD Exposed	Mean + SD Controls	p	Sig.
Age	94	$39^{\pm}$ 9	$39^{\pm}$ 9		N.S.
Blood lead	85	$60^{\pm}$ 15	$24^{\pm}9$	<0.0005	Sig.
Ulnar maximum motor conduction velocity	94	$53.4^{\pm}4.1$	$55.6^{\pm}4.3$	<0.0005	Sig.
Median maximum motor conduction velocity	94	$55.9^{\pm}3.9$	$57.3^{\pm}3.9$	<0.01	Sig.
Ulnar % amplitude	94	$92.2^{\pm}7.4$	$92.6^{\pm}9.7$	>0.05	N.S.
Median % amplitude	94	$94.2^{\pm}7.3$	$94.2^{\pm}9.3$	>0.05	N.S.

(from Archibald J, 1976)

The conclusion drawn by Archibald (1976) is that there is evidence of changes in the peripheral nerve function in absence of symptoms of neurological disturbance, and these changes appear only in motor nerves and not in the sensory nerves. There is no correlation between severity of nerve damage and biochemical tests i.e. blood lead, urinary lead, amino-levulinic acid, amino-levulinic acid dehidrase, haemoglobin, free erythrocytes porphyrine and coproporphyrine urine.

The ulnar motor conduction velocity is affected by the length of exposure ($P < 0.05$) but not the median, radial, peroneal motor nerve conduction velocity.

The lack of individual results made impossible a statistical analysis between the performance tests and nerve conduction velocity in Factory I subjects. This does not mean that in the present work we shall not discuss them: on the contrary, our discussion is based on the results in the nerve conduction velocity tests on both factories' subjects, and conclusion will be drawn on both studies on nerve conduction velocity i.e. Archibald's (1976) in Factory I and mine in the present study in Factory II.

In Factory II the nerve conduction velocity test had been performed on 30 exposed and 23 control workers; the parameters measured had been mentioned in chapter 10, section 10.9.3. The results as means and standard deviations for each of the variables in the nerve conduction velocity study in Factory II are given in Table No. 33 (Page 209).

The mean maximum motor conduction velocity in the median nerve of the exposed muscle action potencial is slower with 1.4m./sec. than that

TABLE 33 Ulnar and median motor conduction velocity, mean and standard deviations in Factory 11 subjects

Nerve	Groups of subjects	No. of subjects	Maximum motor conduction velocity m/sec.		Amplitude wrist mV		Amplitude elbow mV		Elbow/wrist %	
			Mean	SD	Mean	SD	Mean	SD	Mean	SD
MEDIAN	EXPOSED	30	55.8	4.7	12.1	3.6	11.5	3.6	94.6	6.5
	CONTROLS	23	57.2	3.1	14.2	3.1	13.5	2.9	95.4	5.4
ULNAR	EXPOSED	30	54.7	4.9	10.9	3.0	9.8	3.0	90.1	8.3
	CONTROLS	23	56.6	3.4	11.4	2.7	10.3	2.3	91.6	6.4

of the controls, the mean amplitude of muscle action potential when stimulating at the wrist is with 2.1 m.v. bigger in controls than the exposed, and when stimulating at the elbow is 2 m.v. bigger in the controls than the exposed; the percentage elbow/wrist has the mean with 0.8% bigger in controls than the exposed.

The mean maximum motor conduction velocity in the ulnar nerve of the exposed is slower with 1.9 m/sec. than that of the controls; the mean amplitude of action potential when stimulating at the wrist is with 0.5 mv. bigger in the controls than in the exposed; and when stimulating at the elbow, is with 0.5 mv. bigger in the controls than the exposed; the percentage elbow/wrist has the mean with 1.5% bigger in controls than the exposed.

In Table No. 34 (Page 211) is shown that a T-test had been carried out for analysing the above differences and had been found statistically significant ($P < 0.05$) level only for the median nerve for the amplitude of the muscle action potential when stimulating at the wrist and at the elbow. The association of nerve conduction velocity parameters with age, length of employment, blood lead, urinary lead and amino-levulinic acid in urine were analysed by calculating the correlation coefficient for exposed and control workers in Factory II.

Table No. 35 (Page 212) shows the product moment correlation coefficients among nerve conduction velocity parameters and age, length of employment, blood lead, urinary lead and amino-levulinic acid in urine; Table No. 36 (Page 213) shows product moment correlation coefficients between nerve conduction velocity parameters and performance

TABLE 34 The "t" test for ulnar and median motor conduction velocity
in Factory II subjects

Nerve	Groups of subjects	Maximum motor conduction velocity	Amplitude wrist	Amplitude elbow	Elbow/wrist %
MEDIAN	Exposed & controls	1.21519	2.20123 $P < 0.05$	2.14369 $P < 0.05$	0.47015
ULNAR	Exposed anc controls	1.56202	0.61901	0.65302	0.70587

TABLE 35 The product moment correlation coefficients between nerve conduction velocity parameters and age, blood and urinary lead, amino-levunic acid in urine

Variable	MEDIAN Motor conduction velocity E	C	Amplitude wrist E	C	Amplitude elbow E	C	Elbow/wrist % E	C	ULNAR Motor conduction velocity E	C	Amplitude wrist E	C	Amplitude elbow E	C	Elbow/wrist % E	C
Age	-.60+ ***			-.31			-.23	.?7 ***	-.36+ *		-.50+ **	-.21	-.49+ **	-.29		.26
Length of employment	-.44+ **			-.59			-.40+ *			.58						
Blood lead			-.24		-.24				-.22				-.22	.22		
Urinary lead		.37							-.22							
ALA in urine		.43 *							-.24							-.28

Legend: E = exposed subjects
         C = controls
         * significant at 0.05 level
        ** significant at 0.01 level
       *** significant at 0.001 level
         + correlate in the right, expected direction

TABLE 36 The product moment correlation coefficients between nerve conduction velocity parameters and performance tests

	Median Motor conduction velocity E	Median Motor conduction velocity C	Median Amplitude wrist E	Median Amplitude wrist C	Median Amplitude elbow E	Median Amplitude elbow C	Median Elbow/wrist % E	Median Elbow/wrist % C	Ulnar Motor conduction velocity E	Ulnar Motor conduction velocity C	Ulnar Amplitude wrist E	Ulnar Amplitude wrist C	Ulnar Amplitude elbow E	Ulnar Amplitude elbow C	Ulnar Elbow wrist % E	Ulnar Elbow wrist % C
Adding test — time															.30	.44*
errors								-.37								.41
Tapping double 60": latches bridge hits		.35		.36		.36										
Tapping single – No. of taps															-.30	
Grip strength Endurance	-.33						-.37									
One-hole No. of pins grasp positioning									.33	.43*					-.32	
Reaction time arm	.41														.53	
Mx.slope arm			.41+*													
Frequency arm				.43+*		.39			-.43*						-.31	
Reaction time leg										-.42+*				-.38	-.46+**	-.35
Mx.slope leg					.41+			-.38								
Frequency leg																
Reaction time visual	-.44+**	-.41	-.30			-.30		-.37	-.41+**	-.45+*					-.34+*	
Mx.slope visual																
Frequency visual														-.31	.35	

legend: E = exposed.   C = controls.   * significant at 0.05 level.   ** significant at 0.01 level
+ correlate in the right expected direction

tests. For the sake of clarity only correlations of ±20 and over are shown in both these tables.

The significant correlation coefficient which follow the right direction (Appendix No. 2 for the expected sign of correlatins) was found only in the exposed group, between age and median motor conduction velocity (P$\leq$ 0.001), age and ulnar motor conduction velocity (P$<$0.05), age and ulnar amplitude muscle action potential when stimulating at the wrist and at the elbow (P$<$0.01). (Table No. 35) (Page 212).

The length of employment had been found correlated in the right direction, in the exposed group with median motor conduction velocity (P$<$0.01) and with median percentage of amplitude elbow/wrist (P$<$0.05) (Table No. 35).

No right significant correlations were found among nerve conduction velocity parameters and biochemical tests (Table No. 35). Table No. 36 (Page 213) shows that only five of the performance variables are right significantly correlated with some of nerve conduction parameters: maximum slope arm with median amplitude when stimulating at the wrist (P$\leq$ 0.05) in the exposed, frequency arm with median amplitude when stimulating at the wrist (P$<$0.05) in the controls, reaction time leg with ulnar motor conduction velocity (P$<$0.05) in the controls and with ulnar motor conduction velocity (P$<$0.05) in the controls, and with ulnar percentage of amplitude elbow/wrist (P$<$0.01) in the exposed, maximum slope leg with median amplitude when stimulating at the elbow (P$<$0.05) in the exposed, reaction time visual with median motor conduction velocity (P$<$0.01), ulnar motor conduction velocity (P$<$0.05), ulnar percentage of amplitude elbow/wrist (P$<$0.05) all in the exposed

and with ulnar motor conduction velocity (P < 0.05) in the controls.

As it can be seen in Tables 35 and 36, no constant right significant correlation could be found between all nerve conduction velocity parameters and age, length of employment, biochemical tests and performance tests, therefore no further statistical analysis was considered necessary.

12. DISCUSSION

12.1 Introduction

The primary question which the present study has attempted to answer is "do changes in nerve conduction velocity resulting from lead exposure produce a reduction of functional capacity as indicated by the performance of selected behavioural tests?".

Repko and co-workers in 1974 reported the results of a similar study to the present one, in which they studied human performance in relation to biochemical changes. The factory workers they tested had blood lead levels above those found in the present study; a third of that group had blood levels above 70ug/% and only this third presented some changes in performance. The nerve conduction velocity was not tested.

Fullerton and Harrison (1969), Catton et al (1970), Seppalainen et al (1972), Mostafa et al (1972), Vasilescu (1973) and Boothby (1974) all reported studies of nerve conduction velocity on workers with long history of exposure to lead. Their subjects had a high exposure to lead, with a majority above 80ug/%. From Table 3 (Page 58) it can be seen

that Fullerton (1969), Catton et al (1970), Mostaffa et al (1972)
and Boothby (1974) did not find a slowing in motor conduction velocity
but did find some other electrophysiological changes such as a low
percentage of amplitude elbow/wrist in exposed subjects or an increase
of distal latency. None of these investigators studied the performance
of their subjects and so were not in a position to relate their findings
on nerve conduction velocity to performance.

The only study in which the blood lead values are similar to those
found in the present work is that of Seppalainen et al (1975) who
performed nerve conduction velocity on lead exposed subjects and found some
slowing in motor conduction velocity but she did not perform tests of
performance.

Thus there appears to be no information from published studies
involving all three categories of tests, biochemistry, nerve conduction
velocity and performance of lead exposed workers.

One of the problems in the present study was to define or
identify the point, in terms of blood lead values, below which adverse
changes in performance and wellbeing are unlikely to occur.

The *other* behavioural studies on factory workers which have been reported
in this thesis are open to the criticism that the work force of exposed
and control groups were not comparable in respect of age, length of
employment and social background; the work force may be stratified in
relation to ability and lead exposure and such stratification, if it
does exist, is going to affect those studies of behavioural effect in
which blood lead is around the threshold.

Data from a total of 206 industrial workers from two different lead

battery factories were compiled for analysis in this study. The
workers were selected on a voluntary basis, the exposed and control
groups were matched for sex, age, race, length of employment, weight,
height and education. In Appendix 5 (Page 241). it can be seen that the
present study subjects are similar in terms of age and length of exposure
to subjects used in similar studies.

If the observed changes in biochemical parameters and nerve conduction
velocity are indicative of adverse effects on health and performance
it would be expected that correlations should exist between biochemical
and nerve conduction velocity changes and performance tests; the
correlations should lie in a predicted direction as can be seen in
Appendix 2 (Page230). In view of the large number of comparisons that
can be made between biochemical, neurological and behavioural parameters,
significant correlations are going to appear by chance alone. The
correlations, however, should show a constant pattern and trend in the
expected direction which fits the hypothesis that lead exposure influences
nerve conduction velocity and biochemical parameters and will produce
a decrement in performance ability and health.

12.2. Clinical symptoms

A comparison of subjective symptoms between factories and within
factories has indicated that both exposed and control subjects from
Factory I are more irritable and nervy than subjects from Factory II.
Insomnia and vertigo seem to affect more of the exposed groups of
Factory I (Table 12 - Page 160). The problem which arises in judging
these symptoms in this group of workers is that of attributing them to

lead or to environmental factors such as noise, vibrations, temperature, dust, carbon monoxide or to other factors such as drinking and smoking.

To exclude the environmental factors a simultaneous study of the environment in both factories should have been performed. The fact that headache seems to be equally distributed in both factories' populations is an indication that either environmental factors or lead is involved, and not the drinking and smoking which both appear more heavily in Factory I compared to Factory II (Tables 13 & 14 - Pages 162 & 163). Symptoms such as numbness in arms and legs, difficulty in running and walking, grasping and lifting objects affect the exposed workers in nearly equal numbers in both factories. In judging these symptoms the incipient peripheral neuropathy should be taken into account; had the nerve conduction velocity parameters shown significant differences between exposed and controls in both factories or significant correlations with biochemical parameters these symptoms should have been attributed to an incipient neuropathy; in view of the small changes found in nerve conduction tests these symptoms are not considered to be associated with a neuropathy.

12.3. Biochemical tests

As it was mentioned, a pattern of significant expected correlations should emerge before an association between biochemical tests and performancecan be considered to have been demonstrated.

Out of 19 variables analysed for correlations blood lead - performance, lead in blood is only correlated with one-hole test time for positioning the pins in Factory I and frequency leg in Factory II.

Similarly urinary lead and amino-levulinic acid failed to produce a systematic relationship with performance measurements or nerve conduction velocity. Urinary lead is correlated significantly with only 3 out of 19 variables of performance (maximum slope leg & visual and grip strength) and only in workers from Factory 11. There were no correlations between urinary lead and nerve conduction velocity variables (Table 35 - Page 212).

Out of 19 performance variables, amino-levulinic acid in urine only correlates with one (tapping double plates 60" - bridge hits) in Factory I; no correlation could be find with nerve conduction velocity (Table 35).

Results similar to these obtained in the present study for the two urine measures have been reported by Repko et al (1974) and Archibald (1976).

12.4. Performance tests

The performance tests employed in this study attempted to determine if occupational exposure to lead has an affect on intellect (adding test), neuromuscular functions, psychomotor test such as reaction time, grip strength, endurance, tapping speed, eye-hand coordination (one-hole test) and tremor.

The performance has been correlated with biochemical tests, age, length of employment, weight, height and with nerve conduction velocity.

In evaluating these results it must be borne in mind that some tests may be related and therefore give similar results. For example, there are statistically significant correlations between the adding test - time to perform and the adding test - number of errors ($R=0.28$), tapping single plate 60" - number of taps and tapping double plates 60" - number of latches ($R=0.30$), visual reaction time and arm reaction time ($R=0.30$),

but none of these correlations is very large. Some unrelated
correlations also appeared, as with adding test-time to perform and tapping
single plate 60" - number of taps (R=0.30), adding test - number of
errors and arm reaction time (R=0.25), but again they are not very large.

From the study of correlations between biochemical tests (blood
lead, urinary lead and ALA) and performance tests it was revealed that
no correlation could be found between these groups of tests (Table 20)
(Page 173). This finding is similar with that of Repko et al (1974)
who found no dose response relationship for biochemical and performance
tests.

The associations between performance and physical characteristics
(age, weight, height and length of employment) (Table 21) Page 175)
indicated that performance tests such as one hole - number of pins,
reaction time arm, leg and visual, showed consistent and statistically
significant correlations with age, while grip strength, maximum slope
to leg and visual stimulus showed constant statistically significant
correlations with both age and wei ht: the maximum slope achieved
in response to an arm stimulus showed statistically significant correlations
with age, weight and height. It can be concluded from the above findings
that the tests are therefore sufficiently sensitive to identify the
expected effects of age, weight and height.

Repko et al (1974) reported in their study that the age and level
of education contributed significantly to the observed levels of
performance i.e. age was a significant predictor of criterion on scores
on blinking lights and both age and level of education were significant

factors for most of arithmetic computation measures.

Length of employment showed a confused picture when analysed in relation with performance, therefore it was analysed in relation with age by partial regression coefficient and was found to be statistically significantly related to tapping single plate 60" - number of taps, reaction time arm and visual in Factory I exposed. None of the partial regression coefficient was statistically significant in Factory II exposed (Table 28) (Page 189).

The associations between performance and nerve conduction velocity were expected to show a definite pattern i.e. the maximum motor conduction velocity and the percentage of amplitude elbow/wrist in ulnar and median nerves would be correlated significantly with the majority of performance tests. As Table 36 (Page 213) shows, no constant significant correlation pattern emerges for the Factory II people. Thus it can be concluded that the results obtained do not indicate that a slowed nerve conduction velocity of the magnitude found in both groups of factory workers (Tables 32 and 33) (Pages 207 and 209) is associated with any decrement in performance; nerve conduction velocity low with 1.4-2 m/sec. are of doubtful value in determining threshold limit values of lead. A study of people with peripheral neuropathy of other etiology than lead and with large nerve conduction changes (10-15m/sec.) and tested for performance should help to clarify the value of nerve conduction velocity changes in relation to performance.

One of the most sensitive psychomotor test, tremor, tested for the four types of tremor, did not bring more positive findings for the

lead exposed groups.   In Figures 41-44 (Pages 203-206) it can be seen that virtually no significant differences appear to sustain the point of finding more amount of tremor in exposed than in controls.   Indeed, the large amount of data collected for the four tremors should be analysed in a separate work, in search of positive findings.

12.4.1. Evaluation of performance tests used in the present study

The six performance tests used in this study (Adding, Tapping, One-hole, Reaction time, Grip strength and Endurance) proved to be repeatable, acceptable and practical.

Repeatability

Out of 19 variables analysed from the six performance tests, 12 were found not statistically significant between groups;   in the absence of changes due to a toxic substance, in this instance lead, the results came similar and a difference could not be detected. In spite of the fact that the tests were carried out at a difference of six months between factories, the results were similar.

The statistically significant differences obtained for the other 7 variables (tapping double plate 60" - no. of bridge hits, tapping single plate 60" - no. of taps - only for exposed, one hole-grasp time, reaction time arm and visual),an explanation for lack of repeatability of results could be given by the motivation for performing better or worse;   another possibility is the difference of environmental conditions of experiment between factories i.e. Factory II allocated a smaller room for testing which was located near a computer which sometimes produced noise when operated.

The repeatability of tests was also found when the results obtained from the TUC Institute of Occupational Health pilot population were

compared with those of office workers Factory I, taken as the group to match the pilot subjects, (Appendix 6)

Acceptability

The acceptability of performance tests was proved by the good response from the subjects in coming to be tested without resentment; on the contrary, they were very eager to perform at their best possibilities, and this could be seen in the tendency of some tests, such as reaction time, grip strength and endurance, to be better in exposed than controls.

The tests were not time consuming, so that the management of both factories agreed in carrying out the present study in working time, and this was also convenient for the worker, who did not need to spend his free time for the tests.

Because no drastic procedure was used in testing (i.e. high voltage, too many electrical stimuli, needle electrodes) the workers declared that they enjoyed participating in this experiment, and asked many questions related to the testing procedures.

Practicability

The equipment used can be easily transported to different working places. Once a battery of performance tests is collected, it can be

used in testing groups of people exposed to many toxic substances, such as solvents, alcohols, heavy metals etc.

Operating the tests is a clean procedure which does not involve the use of chemical reactives or expensive materials - only graph paper and polaroid photographs.

12.5. Nerve conduction velocity

The parameters obtained from nerve conduction velocity study (Table 33) (Page 209) have been analysed for associations with biochemical parameters (Table 35) (Page 212) and with performance parameters (Table 36) (Page 213).

The reason for performing the analysis only in Factory II workers - exposed and controls have been explained in chapters 10, Sections 10.2. and Chapter 11 Section 11.6.

The results in mean motor conduction velocity for the ulnar and median nerves in dominant forearm seem to be very similar in Factory I (Table 32) (Page 207) and in Factory II (Table 33) (Page 209); Archibald (1976) reported a mean difference of 2.2m/sec. for ulnar between exposed and controls in Factory I and the difference found in Factory II was 1.9m/sec.; for median nerve Archibald reported a difference in means between Factory I exposed and controls of 1.4m/sec. and the difference found in Factory II was 1.6m/sec. The figures presented by Archibald (1976) come to be statistically significant (P$<$0.0005) for ulnar and (P$<$0.01) for median in Factory I while in Factory II the "t" test did not come significant due to less number of people tested than that of Factory I.

It is interesting to note the negative finding, in terms of statistical significance of the most sensitive index - the percentage amplitude elbow/wrist (Fullerton and Harrison 1969, Catton et al 1970, Seppalainen et al 1972, 1975) as a measure of velocity of slow fibres, in both factories (Tables 32 and 33) (Pages 207 and 209).

The associations between nerve conduction velocity parameters and biochemical test showed no statistical significant correlations (Table 35) (Page 212) in Factory II and this is similar to Archibald (1976)

report for Factory I. Also, this is similar to other results, such
as Catton et al. (1970) and Seppalainen et al (1972,1975).

Associations between nerve conduction velocity parameters and
age showed statistically significant correlations in the Factory II
exposed groups (Table 35) for both nerves; this is a similar result
with Archibald (1976) in Factory I who reported decreases in motor
conduction velocity as the age increases, and with results of Thomas
and Lambert (1960), Wagman & Lesse (1952), Norris et al (1953) and
Seppalainen et al (1975).

Length of exposure showed a tendency towards significant correlations
with median parameters in exposed Factory II but not for the ulnar nerve;
this comes contrary to Archibald (1976) finding in Factory I, who
reported significant correlation with ulnar parameters, but not with
median parameters.

13. CONCLUSION

The present study of performance, neurophysiological, biochemical,
subjective clinical symptoms, behaviour, indicated that in occupationally
lead exposed people over a blood lead range of 13-79ug/100ml. a dose
response relationship between performance, nerve conduction velocity,
urinary lead and ALA could not be established.

The changes in nerve conduction velocity statistically significant
in one Factory but not in the other were not big enough to correlate
with biochemical or performance tests.

In view of the above findings, it can be concluded that there is no
evidence that blood lead values up to 79ug/100ml. are associated to
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APPENDIX 1 - List of variables analysed in the present work

The variables entered in the punched cards.

Population physical characteristics -

1. Age (years)

2. Weight (kg.)

3. Height (cm.)

4. Length of employment (years)

Biochemistry tests -

5. Blood lead (ug/100ml.)

6. Urinary lead (ug/litre)

7. Amino-levulinic acid in urine (mg/litre)

Performance tests -

8. Adding test - time to perform (minutes)

9. Adding test - number of errors

10. One hole test - number of pins inserted in the first 30 sec. lowest

11.   "   highest

12.   "   60" sec. lowest

13.   "   " highest

14.   "   the seven trials - total

15.   "   " lowest

16.   "   " highest

17. One hole test - time corresponding to the grasp (sec) - total

18.   "   " lowest

19.   "   " highest

20. One hole test - time corresponding to the position (sec.) total

21.   "   " lowest

22.   "   " highest

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14. " the seven trials - total

15. " " lowest

16. " " highest

17. One hole test - time corresponding to the grasp (sec) - total

18. " " lowest

19. " " highest

20. One hole test - time corresponding to the position (sec.) total

21. " " lowest

22. " " highest

51. Reaction time leg, volts for stimulation

52. Reaction time leg I trial (millisec.)

53.   "   II   "

54.   "   III   "

55.   "   mean of three trials

56. Maximum slope leg I trial (volts)

57.   "   II   "

58.   "   III   "

59.   "   mean of three trials

60. Frequency leg, I trial (Hertz)

61.   "   II   "

62.   "   II   "

63.   "   mean of three trials

64. Reaction time visual I trial (millisec.)

65.   "   II   "

66.   "   III   "

67.   "   mean of three trials

68. Maximum slope visual, I trial (volts)

69.   "   II   "

70.   "   III   "

71.   "   mean of three trials

72. Frequency visual I trial (Hertz)

73.   "   II   "

74.   "   III   "

75.   "   mean of three trials

76. Grip strength (kg)

77. Endurance (sec.)

Nerve conduction velocity -

78. Ulnar nerve - motor conduction velocity (Metres/second)

79. Ulnar nerve - amplitude elbow (millivolts)

80.   "   - amplitude wrist (millivolts)

81.   "   - percentage of amplitude elbow/wrist (%)

82. Median nerve - motor conduction velocity (metres/second)

83.   "   - amplitude elbow (millivolts)

84.   "   - amplitude wrist (millivolts)

85.   "   - percentage of amplitude elbow/wrist (%)

Tremor

Variables Nr. 86-149 represent the mean power for postural tremor. The spectrum of frequency is 0.5-32 Hertz and the mean value of power was taken for each step of frequency of 0.5 Hertz. i.e.

Variable 86 = 0.05 Hz .... Variable 149 = 31.5-32 Hz.

Variables Nrs. 150-213 represent the mean power for intentional tremor i.e.

Variable Nr. 150 = 0.05 Hz............... Variable Nr. 213 = 315.-32 Hz.

Variables Nrs. 214-277 represent the mean power for balance board tremor when the eyes are open i.e.

Variable Nr. 214 = 0.05 Hz............... Variable No. 277 = 31.5-32 Hz.

Variables Nrs. 278-341 represent the mean power for balance board tremor when the eyes are shut i.e.

Variable Nr. 278 = 0.05 Hz.............. Variable Nr. 341 = 315.-32 Hz.

APPENDIX 2 - Table of expected sign of correlation coefficients.

Performance tests	Age	Length of employment	Blood lead	Urinary lead	ALA	All nerve conduction velocity parameters
Adding test - time	+	+	+	+	+	-
- errors	+	+	+	+	+	-
Tapping double plates 60" latches	-	-	-	-	-	+
bridge hits	+	+	+	+	+	-
Tapping single plate 60" Nr. of taps	-	-	-	-	-	+
Grip strength	-	-	-	-	-	+
Endurance	-	-	-	-	-	+
One-hole Nr.of pins	-	-	-	-	-	+
Grasp	+	+	+	+	+	-
Positioning	+	+	+	+	+	-
Reaction time arm	+	+	+	+	+	-
Maximum slope arm	-	-	-	-	-	+
Frequency arm	-	-	-	-	-	+
Reaction time leg	+	+	+	+	+	-
Maximum slope leg	-	-	-	-	-	+
Frequency leg	-	-	-	-	-	+
Reaction time visual	-	+	+	+	+	-
Maximum slope visual	-	-	-	-	-	+
Frequency visual	-	-	-	-	-	+

SURVEY OF WORKERS EXPOSED TO LEAD

Date (time of survey) ....

Survey No ....

Survey conducted by ....

Section I: Personal history

1. Surname (Block letters) ....

    Forename ....

2. Age (In years) ....

Section II: Occupational history

1. Present occupation ....

2. Department ....

3. Shift (present) ....

    What time does it start ....

4. Years spent in present job ....

5. Any previous work with lead? (State duration and specify) ....

    ....

    ....

    ....

    ....

		YES	NO

1. Has there been any change in your temper in the last six month?   ....

    a)   If yes, do you quarrel more?   ....

    b)   If yes, where:

             - at work?   ....

             - at home?   ....

2. Have there been any difficulties in getting to sleep in the last six month?   ....

    If yes:

    a)   What time do you go to bed? ....

    b)   On average does it take you 1/4, 1/2, 1/3, 1 hour or more to get to sleep?

        ....

    c)   When do you wake up? ....

3. Do you suffer from headache in the last six month?   ....

    If yes:

    a)   in the morning?   ....

    b)   at the end of the day?   ....

    c)   during the week?   ....

    d)   at weekends?   ....

    e)   how do you define it: dull?   ....

                              throbbing?   ....

	YES	NO

4. In the last six month, have you had: vertigo?   ....

                                          unsteadiness?   ....
                                          (muziness)

If yes, when? ....

....

Section IV: Disturbances of extremities

1. Do you feel numbness in the last six month?   ....

If yes:

      - is it constant?   ....

      - does it appear sometimes?   ....

2. In the last six month have you had difficulties in:

                                      running?   ....

                                      walking?   ....

                                lifting objects? ....

                                  grip strength?   ....

If yes, when? ....

....

3. Do you feel cold in the hands or feet when others do not,
especially in the last six month?   ....

4. Do you suffer from cramps in the legs:

         at night ?   ....

         by day?   ....

If yes, for how long? ....

5. Tremor (to be observed by surveyor) ....

....

....

....

Section V. Disturbances of digestive tract.

1. In the last six month have you lost on weight?   ....

2. In the last six month have you suffered from:

        - diarrhoea   ....

        - constipation   ....

        - nausea   ....

        - vomiting   ....

        - abdominal pain   ....

3. Have you noticed, in the last six month, any change in
your appetite?   ....

If yes, describe: ....

....

....

Section VI.   Disturbances of eyes

1. Has your vision become blurred in the last six month?   ....

2. Have you noticed any other defect in your sight in
    the last six month?   ....

    If yes, describe: ....

    ....

    ....

    ....

Section VII.   Smoking

1. Do you smoke now?   ....

2. Please, give details of present smoking habits:

            -    manufactured cigarettes no/day?   ....

            -    hand-rolled cigarettes oz/week?   ....

            -    pipe tobacco oz/week?   ....

            -    cigars no/day?   ....

3. At what age did you start smoking? ....

4. Have you given up smoking?   ....

5. How long ago did you give up smoking cigarettes? ....

....

Section VIII.   Drinking

1. Do you ever take an alcoholic drink?   ....

2. What is your usual drink?

        Beer? ....

        Spirits? ....

        Wine? ....

        Fortified wine? ....

3. During the past week what quantity have you consumed? ....

....

....

....

....

Table 6

					TOTAL
16	22	77	94	39	
84	42	17	53	31	
63	01	65	78	59	
33	21	12	34	29	
57	60	86	32	44	

Table 7

					TOTAL
49	54	43	54	82	
57	24	55	06	88	
16	95	55	67	19	
78	64	56	07	82	
09	47	27	96	54	

Table 8

					TOTAL
17	37	93	23	78	
77	04	74	47	67	
98	10	50	71	75	
52	42	07	44	38	
49	17	46	09	62	

Time Started _____

Time Finished _____

Table 9

87	35	20	96	43	
21	76	33	50	25	
12	86	73	58	07	
15	51	00	13	42	
90	52	84	77	27	

Table 10

					TOTAL
84	26	34	91	64	
83	92	12	06	76	
44	39	52	38	79	
77			76	54	
08	02	73	43	28	

Table 11

					TOTAL
18	18	07	92	46	
26	62	38	97	75	
25	12	40	64	74	
52	36	23	7	95	
37	85	94	35	12	

Table 12

					TOTAL
44	17	16	58	09	
84	16	07	44	99	
82	97	77	77	81	
50	92	26	11	97	
83	39	50	08	30	

Table 13

					TOTAL
79	83	86	19	62	
83	11	46	32	24	
07	45	32	14	08	
00	56	76	31	38	
42	34	07	96	88	

Time Started _____

Time Finished _____

Table 14

					TOTAL
06	76	50	03	10	
20	14	85	88	45	
32	98	94	07	72	
80	22	02	55	55	
54	42	06	87	98	

Table 15

					TOTAL
55	25	64	05	05	
10	93	72	88	71	
93	85	79	10	75	
86	60	42	04	53	
35	85	29	48	39	

Table 16

					Total
40	29	17	12	13	
56	62	18	37	35	
99	49	57	23	47	
16	08	15	04	72	
31	16	93	32	43	

Table 17

					Total
40	33	20	38	26	
96	83	50	84	40	
88	45	92	93	72	
33	27	14	34	09	
50	27	89	87	19	

Table 18

					Total
13	89	51	03	74	
94	12	25	93	47	
16	44	56	16	00	
45	59	34	68	49	
20	15	37	00	49	

Time Started _____

Time Finished _____

Table 19

					Total
17	76	37	15	04	
70	33	24	03	54	
04	43	18	66	79	
12	71	07	34	45	
52	85	66	60	41	

Table 20

					Total
07	74	21	19	30	
97	77	46	44	80	
94	77	24	21	90	
99	27	72	95	14	
38	87	88	11	80	

APPENDIX 5 - Table showing results of published studies from which a comparison
could be made with the present work in terms of biochemical tests, age,
length of employment, weight and height

Authors	Tests performed	No. of subjects	Age	Weight	Height	Length of employment years chronic	Blood lead ug.%	Urinary lead ug./l.	ALA mg./l
Sessa (1965)	N.C.V.	20							
Fullerton and Harrison (1969a)	N.C.V.	19				5-13	>80		
Fullerton (1969b)	N.C.V.	5				5-13	>80		
Catton et al (1970)	N.C.V.	19	19-44			1-1	40->120		
Seppalainen (1972)	N.C.V.	39	18-63			2.5-22	40->80		
Seppalainen (1975)	N.C.V.	26	35-50			1-17	28-65		7.4
Mostafa (1975)	N.C.V.	20	26-55			1-36	21-76	50-145	
Vasilescu (1973)	N.C.V.	50	41.5			Chronic	27-180	60-1875	
Boothby (1974)	N.C.V.	1	55			30	40-80	>350	6-20
Repko et al (1974)	Performance	316	18-64	105-270 pounds	60-76 inches	1-29	<39->100	4-1247	

Legend: N.C.V. = Nerve conduction velocity

APPENDIX 6 - Table showing means and standard deviations of age, weight height and performance in T.U.C. Institute of Occupational Health pilot subjects and office controls in Factory I

Variable	12 Pilot subjects mean	SD	49 Office controls mean	SD
Age	35.7	13.0	38.2	9.7
Weight	72.5	4.7	74.9	8.0
Height	174.2	3.9	176.0	6.4
Adding test time	14.1	6.2	14.7	5.1
errors	4.0	3.0	4.4	3.2
Tapping double plates 60" latches	130.7	14.2	133.9	17.5
Bridge hits	8.9	7.3	9.9	9.2
Tapping single plate 60" No.of taps	348.8	25.2	357.6	28.1
Grip strength	54.5	8.0	58.1	9.0
Endurance	28.9	7.2	30.7	14.5
One-hole test pins	290.5	33.3	294.1	36.2
grasp	59.1	24.3	60.7	22.2
positioning	83.3	7.2	88.6	10.5
RT arm	122.5	25.2	127.2	26.9
MS arm	6.2	1.5	6.7	1.6
Frequency arm	3.4	0.8	3.4	0.6
RT leg	142.7	30.1	149.4	34.3
MS leg	6.8	1.2	7.1	1.4
Frequency leg	3.3	0.5	3.4	0.6
RT visual	133.6	15.3	137.3	22.0
MS visual	6.8	1.5	7.0	1.4
Frequency visual	3.4	0.3	3.2	0.6