STUDIES IN LEAD ABSORPTION

AND LEAD POISONING

by

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CONTENTS

This thesis is dedicated to

my father,

the late James Chalmers M.D.

CONTENTS

PREFACE.

The work described in this thesis was undertaken by the author when holding the following appointments:

(1)   Senior Assistant Resident Physician, the County of Lanark Infectious Diseases Hospital, Motherwell.

(2)   Extra Dispensary Physician and Clinical Assistant, the Western Infirmary, Glasgow.

(3)   Assistant Director in the Department of Clinical Investigations and Research, University and Royal Infirmary, Manchester.

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The author takes great pleasure in acknowledging his indebtedness to:

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The nursing staff of the Western Infirmary, Glasgow, and other institutions.

The lead workers who willingly offered themselves for examination and for test purposes.

The results recorded in Tables IV, V and VII have been accepted for publication by the 'Lancet' (Chalmers, 1940) and are at present in the press.

Dr. S. L. Tompsett performed many of the lead analyses of biological materials in cases 1, 2, 4 and 7 to 11; certain of these results have already been incorporated in work already published (Chalmers and Tompsett, 1938. Tompsett and Chalmers, 1939).

Apart from these, and such tests as serum calcium estimations and Wassermann reactions, all the investigations recorded - both clinical and laboratory - have been personally performed.

INTRODUCTION.

1. Historical.

Lead intoxication, also known as plumbism or saturnism, is still the commonest form of industrial poisoning, although preventive measures have greatly reduced the incidence of the disease. Non-industrial lead poisoning also occurs from such diverse sources as water supplies, food, beverages, drugs and cosmetics.

The disease presents a problem to public health authorities, physicians and surgeons, pathologists, biochemists and analysts, as well as to employers, employees and medico-legists.

The disease now known as lead poisoning was recognised by the ancients, Hippocrates (c.420 B.C.) being probably the first to recognise it. He described the occurrence of severe colic in a man who extracted metals. Nicander (c.200 B.C.) observed the relationship of constipation, abdominal pain and pallor of the skin to the action of lead; Horace (c.25 B.C.) and Vitruvius (c.20 B.C.) wrote on the disadvantages of water delivered through lead pipes, and Pliny (c.60 A.D.) mentioned the noxious qualities of lead fume. Alderson (1852) reviewing the history of plumbism, quotes Dioscorides (c.77 A.D.) as noting paralysis and delirium being associated with lead intoxication.

Crato (c.1600 A.D.) attributed the colic which was common in Moravia to the drinking of "falsified wine", and in 1616 Citois,

a physician of Poitiers mentioned bad wine which had been treated with lead "as a sweetening agent" as the cause of colic (colica Pictonum) in that district, and gave a detailed clinical description of lead poisoning, although he attributed the illness to the acid of the wine and not to the lead.

In 1745 Huxham described 'Devonshire colic', the symptoms of which were identical with those of lead poisoning, and the cause of this was traced by Baker (1767) to the lead employed in the manufacture and storage of cider.   Grisolle (1836) described the "blue line on the gums" met with in lead poisoning, although this sign is frequently referred to as the 'Burtonian line' following the description by Burton in 1840.   A detailed clinical account of plumbism was published in 1839 by Tanquerel des Planches, who gave the results of experiments carried out on animals poisoned with lead.

Cases of industrial plumbism were very frequent in the 18th and 19th centuries, but owing to legislation, improved working conditions and an increasing interest in preventive medicine the incidence has shown a very great fall in the last forty years. Among authorities working in the field of prevention of lead poisoning may be mentioned Legge and Goadby, Oliver, Lane and Hunter in England, Melliere in France, Teleky in Germany and Aub and Hamilton in the

United States.

The pathology and haematology of lead poisoning have also
been extensively studied by these workers and the biochemistry of
lead up to 1925 was reviewed by Aub, Fairhall, Minot and Retznikoff
(1926), who themselves produced valuable information on the subject.
More recently, papers by Kehoe, Thamann and Cholak (1933) and Aub
(1935) in the United States and by Roche Lynch et al. (1934), Tompsett
and Anderson (1935), Monier-Williams (1938) and Tompsett and Chalmers
(1939) working in Britain, have added further knowledge regarding
the biochemical effects of lead.

2.   Incidence of lead poisoning.

Industrial lead poisoning became notifiable in Britain under
Section 73 of the Factory and Workshop Act (1901) and is now notifiable
under Section 3 of the Lead Paint (Protection against Poisoning) Act
(1926) and Section 66 of the Factories Act (1937).

From the results of these notifications the frequency of
the disease in various industries and trades can be studied.   Statistics
are not available for the years before 1900, but Oliver (1914) in his
treatise on the subject, and in a personal conversation with the author
(1939), described the widespread bad working conditions in industry
and the high morbidity in both sexes due to lead intoxication before
the disease became notifiable.   The common occurrence of the disease
in the last century is also recorded by Tanquerel des Planches (1839)
working in France and Putnam (1883) in the United States.

Table I gives statistics of the notifications of industrial lead poisoning obtained from the annual reports of the Chief Inspector of Factories for years between 1900 and 1938. There has been a maintained fall in the incidence of notified cases since the beginning of the twentieth century.

Table I.

Notified cases of industrial lead poisoning.

Year	1900	1910	1920	1930	1935	1936	1937	1938
Cases notified	1058	505	289	265	168	163	141	96

Briefly, the cause for this decline in incidence is due to legislation involving the notification of lead poisoning, improved working conditions and the regular medical examination of lead workers. Details in regard to these factors and a review of the case incidence in various occupations are given in another section of this thesis.

Non-industrial lead poisoning, although by no means as common as the industrial form, usually arises from the ingestion of lead-contaminated water, beverages and food or the accidental or intentional taking of drugs. Unusual cases from other sources have also been reported. Statistics of such cases are not available, but a review of the literature shows that they are by no means rare, even under modern conditions of life. Minot (1938) regards the non-industrial exposure to lead to be on the increase and she stresses the

need for further investigation of the problem.

A review of the subjects of lead poisoning and lead absorption and the results of tests for lead carried out by the author in individuals with no known industrial exposure to lead, asymptomatic lead workers and cases of clinical plumbism of industrial and non-industrial origin are subsequently described in this thesis. Details of experience in prophylaxis and treatment of the disease are also recorded.

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THE PHYSIOLOGY AND BIOCHEMISTRY OF LEAD.

(a) Lead Absorption.

Lead can be absorbed into the system through the respiratory and alimentary tracts and, in certain instances, through the intact skin.

Absorption through the respiratory tract is the most common cause of industrial plumbism. This fact was overlooked for some time, and although Tanquerel (1840) caused experimental lead poisoning in a dog by the tracheal insufflation of minium, it was not until 1909, when Goadby proved the importance of absorption of lead by the lungs, that more stringent measures were taken to reduce the risk of inhalation of lead fume and dust in industry. Further experimental work by Aub, Fairhall, Minot and Retznikoff (1926) has shown the great importance of lead absorption through the respiratory tract and Blumgart (1923), experimenting with dogs prepared by means of a tracheal cannula and ligation of the oesophagus so that no lead could enter the lungs or alimentary tract, showed that lead could be absorbed through the naso-pharynx.

In the above-mentioned experiments symptoms of poisoning developed much more rapidly when lead was introduced into the respiratory tracts of animals than when the same dose was given by mouth. Lead compounds are dissolved in the secretions of the bronchial tree and are absorbed directly into the lung alveoli, although it is possible that absorption by phagocytosis of lead particles may also occur (Aub et alia, 1926).

When lead enters the body through the respiratory tract, absorption occurs directly into the systemic circulation, while that entering through the gastro-intestinal tract may be excreted per rectum without ever being absorbed, or, after absorption, may be taken up by the liver and excreted in the bile without ever having entered the systemic circulation. Thus a proportion of the lead absorbed from the gastro-intestinal tract is confined to a region where it can cause relatively little damage.

In the gastro-intestinal tract, the stomach is chiefly responsible for the solution of swallowed lead particles and absorption, according to Fees (1932), is rapid and takes place in the stomach and upper intestine, although there is not full agreement on this. Lead chromate is very soluble and is rapidly absorbed, being very toxic, as is lead acetate. The less soluble salts such as the carbonates and oxides are, however, fairly readily absorbed from the gastro-intestinal tract. Sulphide of lead is probably only very slowly absorbed as such. Some authorities hold that lead is always absorbed from the gastro-intestinal tract in the form of chloride.

The calcium content of the diet (Tompsett and Chalmers, 1939) and the degree of acidity of the intestinal contents (Tompsett, 1939 b.c.) are important factors concerned with absorption of lead from the gut. A high calcium intake inhibits lead absorption whereas administration of acid increases the amount absorbed. These laboratory findings confirm the opinion of the late Sir Thomas Legge, who advocated the regular intake of milk by lead workers. A high milk

(calcium) diet has the effect of reducing the acidity of the intestinal tract and thus hinders lead absorption.   It also results in lead present in the stomach and intestine being formed into a poorly diffusible colloid state and has the added value of causing absorbed lead to be laid down in osseous tissue where it is relatively non-toxic.

Although, in animal experiments, Sobel, Gawron and Kramer (1938) found that viosterol increased lead absorption, this could not be confirmed by Tompsett (1939) who found lead absorption uninfluenced by the addition of Vitamin D to the diet.

Absorption of lead directly through the intact skin is of very rare occurrence except in the case of organic preparations such as tetra-ethyl lead which are soluble in the natural fats of the skin and are rapidly absorbed.   These preparations are very toxic and quickly cause paralytic and maniacal symptoms.   Some authorities hold that, in these cases, the 'ethyl' group is more poisonous than the lead, although this is a debatable point.

Some cases of poisoning due to hair lotions or cosmetics (Bartleman and Dukes, 1936) have been reported; these, however, are very uncommon.   The experimental work of Fairhall and Heim (1932) who found that persons wearing lead-weighted silk underclothing under extreme conditions of activity and perspiration showed no evidence of lead absorption proves satisfactorily that absorption through intact skin is slight or non-existent.   The application of lead preparations to wounds and raw surfaces has on occasion resulted in toxic symptoms in susceptible individuals but, again, such occurrences are rare.

Experimental work has shown that various forms of lead introduced parenterally into animals quickly bring on symptoms of poisoning, and the work of Blair Bell (1930) and Brookfield (1928) who observed cancer cases under treatment with colloidal lead demonstrated that the effects of lead soon show themselves after parenteral injection.

The lead intake in normal life.

It is now recognised that the normal individual is exposed to, and excretes small amounts of lead with apparent ill-effect. It has also been found, as a result of improved analytical technique, that most human tissues contain traces of lead, the highest concentrations being found in the bones. The source of this normal amount of lead in the human body and of that excreted is food, water and inhaled dust particles.

Food may be contaminated by lead in the following ways:

1. The use of solders, enamels and glazes containing lead, in apparatus and vessels used for the manufacture, storage, transport or cooking of food.

2. The use of ingredients (e.g. food colours) in the production of which materials containing lead have been used or which have been manufactured in lead-lined vessels.

3. The use of insecticides containing lead on fruit and vegetables.

4. The exposure of food to dust containing lead.

5. Shell fish may contain 'natural' lead, presumably extracted from sea water.

The above is a summary from a report by Monier-Williams (1938), who has recently reviewed the question of lead in food and

found that many foodstuffs contain minute traces of lead. On several
occasions he found appreciably higher quantities in certain foods and
food ingredients which he regarded as excessive. As examples of these
he quotes the following:

	Parts per million
Baking powder	7.1
Sardine paste	8.3
Curry powder	21.6
Indian tea (loose)	10.2
Turmeric root	282.5
Damson blue paste (food colour)	337.0
Apple green paste (ditto)	85.0
Apricot yellow paste (ditto)	44.0

He also mentions instances in the past where aerated waters,
beer, cider, acid calcium phosphate and canned foods were found to
contain high amounts of lead, and describes cases where clinical lead
poisoning developed after ingestion of contaminated food. He concludes
that, normally, about 0.2 to 0.25 mgm. of lead is likely to be ingested
daily with food.

Ingleson (1934) reviewing the question of lead in drinking
water, states that any water delivered through lead pipes may be expected
to contain lead, although the amounts present in many cases are so
minute that they can be regarded as insignificant. Opinions vary as to
what should be considered a 'permissible limit' of lead in water. There
is no legal limit. Ingleson quotes Howard as stating that 0.25 mgm. Pb.

per litre is 'poisonous', while other authorities put the limit as
2.0 mgm. Pb. per litre.   Currie (1936) is of the opinion that 0.1
mgm. per litre may be harmless.   Tompsett and Anderson (1935) found
the Glasgow Royal Infirmary supply to contain 0.03 mgm. Pb. per litre
and the author, taking water from house supplies in different parts of
Glasgow, found lead present on every occasion, the amounts varying
between 0.041 to 0.133 mgm. Pb. per litre.   The higher figures were
obtained after the water had been standing overnight in lead service
pipes.   These results and a report of lead poisoning developing from
a private water supply containing 8 mgm. Pb. per litre are considered
in a later section of this thesis.

The amount of lead in any water supply is known to vary
from time to time (Ingleson).   Monier-Williams holds that normally,
amounts up to 0.2 or even 0.25 mgm. Pb. per day may be ingested with
water without ill-effect.   These higher figures, together with his
estimate of the average daily content of lead in food would make a total
lead intake of 0.4 to 0.5 mgm. per day.   Kehoe, Thamann and Cholak
(1935) working in Cincinnati found that an average American diet
contained 0.25 mgm. Pb. per day, and Tompsett and Anderson found
hospital diets to contain 0.22 mgm. Pb. daily.

The third source of lead absorption by the normal individual
is by the lungs.   It seems probable that this may not amount to very
much, but lead dust derived from industrial processes, wear and tear
of paint and exhaust gases from motor vehicles using 'ethyl' petrol
give rise to a small quantity of lead being present in the atmosphere,
more especially in cities.

Bloomfield and Isbell (1935) reported an average of 0.9 mg.
Pb per 10 cubic metres of air in 28 samples of air collected at
congested street crossings in America, and the Departmental Committee
on Ethyl Petrol (1930) found amounts up to 0.65 mg. per cubic metre
of air in an "experimental traffic block" in a tunnel. This was an
extremely severe test, however, and the Committee regarded the risk
of danger from ethyl petrol under ordinary circumstances to be
negligible.

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Methods of lead analysis.

Any method employed for the quantitative determination of lead in food, water or biological materials has to be sensitive and specific, as the amounts to be estimated are, as a general rule, extremely small. Even with improved modern technique errors may occur and the results recorded have to be interpreted bearing this in mind. Much has been done, however, to reduce error to a minimum and this, together with the employment of more uniform technique by various workers, has caused the analytical results to have far greater significance than in the past.

Earlier methods in which small amounts of lead were estimated colorimetrically as the sulphide are not suitable for analysis of biological materials, but may, as will be shown later, prove satisfactory for the quantitative estimation of lead in water. Fairhall (1924) described a method which involves extraction and precipitation of lead as sulphide, formation into chromate, and subsequent colorimetric determination or titration with sodium thiosulphate after the addition of potassium iodide. The quantity of lead in water or urine may be determined by this method, but difficulties arise in the analysis of blood and soft tissues which have a high iron content from which lead has be be separated. Kehoe et al. (1926) used a modification of Fairhall's method, but subsequently (1935) admit that loss of lead occurred during the performance of the tests.

Litzner and Weyrauch (1932, 1933) employed an electrolytic method, but, as was pointed out by Francis, Harvey and Buchan (1929)

such technique usually fails in the presence of relatively large amounts of iron, and hence this method is unsuitable for the analysis of biological materials. Good results from spectrographic technique have been reported by Blumberg and Scott (1935), and micropolarographic methods have also been used.

Chemical analyses, however, are more practicable and the difficulty of interference by iron was overcome by Allport and Skrimshire (1932a). After ashing the material to be tested, they shook up an alkaline solution of the ash with a chloroform solution of diphenyl-thiocarbazone (dithizone). Lead was extracted as a lead-diphenyl-thiocarbazone complex. Iron and other metals, with the exception of bismuth were not extracted if cyanide was present. Difficulties, however, were encountered if the ash solution was not perfectly clear as turbidity due to phosphates prevented a complete extraction of lead. They also found (1932b) that if nitric acid had been used as an oxidant in the process of extraction of lead, this was usually incomplete.

In the final colorimetric or titrimetric estimation of lead, the sulphide reaction, as pointed out by Tompsett and Anderson (1935) is not entirely satisfactory, as bismuth gives the same reaction.

The dithizone method of Allport and Skrimshire was improved by Fischer and Leopoldi (1934) who found that a pink complex was formed when an alkaline solution of a lead salt was shaken up with carbon tetrachloride. After shaking, the carbon tetrachloride layer contained the pink lead complex and also unchanged green diphenylthiocarbazone.

The excess of unchanged dye could be removed by shaking the carbon tetrachloride with 1 per cent potassium cyanide. They finally added weak acid to the pink complex in the carbon tetrachloride, which restored the green colour, and then compared it against a standard in a colorimeter.

Tompsett, in the above quoted paper by himself and Anderson, modified this method and found the pink complex as sensitive to colorimetric estimation as the green and recently (1939a) has published further details of his technique and results. He and the author carried out numerous tests using his method in the Biochemistry Department of the Royal Infirmary, Glasgow, and found it, in the light of present knowledge, to be sensitive, specific and accurate. As the results of the lead analyses subsequently recorded are dependent on this technique, details of the method are described in full.

The colorimetric estimation of lead in biological materials by the dithizone method.

General considerations.

Possible extraneous contamination by lead has to be avoided from the time of obtaining the material to be tested until the final colorimetric estimation.

All reagents used are rendered lead free, and are of 'Analar' standard.

Pyrex glassware (which is a tri-bromo-silicate) is employed throughout. Ordinary glassware may contain lead.

Distilled water is obtained by using a Pyrex glass still, and is alone used during the tests and for cleaning all apparatus.

Ordinary corks and Pyrex ground glass stoppers are used, no rubber tubing or rubber bungs (which may contain lead) being employed.

Stainless steel needles of standard and uniform make (S-B No. 1) are used to obtain the blood samples and are washed and sterilised in distilled water before use. When a 20 ml. syringe has to be employed it is similarly prepared, and the same syringe is used on each occasion.

Urine and water are collected in Pyrex litre flasks or wax-lined bottles. Faeces are collected directly into leadless-glazed containers. Specimens obtained at post mortem are put into Pyrex vessels without the addition of fluid. All materials are kept in a refrigerator until ashed.

(A). Blood.

Collection of the sample.

After careful cleansing of the skin of the forearm (which, to avoid contamination, is most important when dealing with lead workers) and application of spirit, between 20 and 25 ml. of blood are obtained by venipuncture. As a general rule this can be done by inserting a needle directly into a vein and allowing the blood to flow directly into a 30 ml. Pyrex test tube containing a little lead-free potassium oxalate. Should the veins be small, as for example in the case of children, a 20 ml. Record syringe has to be employed. When

the required quantity of blood has been obtained the tube is corked
and shaken to ensure mixing with the oxalate and avoidance of
coagulation.

Reagents ('Analar' standard) required for chemical analysis.

1. Concentrated hydrochloric acid.

2. Concentrated sulphuric acid.

3. Concentrated nitric acid.

4. Perchloric acid.

5. Glacial acetic acid.

6. Ammonia (sp. gr. 0.88).

7. Ether.

8. 10 per cent potassium cyanide - Pb.T. (B.D.H.)

9. 1 per cent potassium cyanide - Pb.T. (B.D.H.)

10. Carbon tetrachloride.

11. 20 per cent sodium citrate (lead free).   This is prepared by
    adding 100 ml. of 1 per cent solution of diphenylthiocarbazone
    in chloroform to a litre of 20 per cent of sodium citrate and
    shaking vigorously, and the then de-leaded citrate removed from
    the chloroform by means of a separating funnel.

        Glacial acetic acid and hydrochloric acid are at times
    found to contain traces of lead and these are de-leaded as
    described above, carbon tetrachloride being used instead of
    chloroform.

12. 1 per cent diphenylthiocarbazone in carbon tetrachloride.

13.   2 per cent diethyldithiocarbamate in aqueous solution.

14.   Standard lead acetate solution.   0.1831 g. of lead acetate

is dissolved in distilled water containing 5 ml. glacial

acetic acid.   The volume is made up to one litre with distilled

water.   1 ml. of this solution is equivalent to 0.1 mg. Pb.

This solution is diluted 1 in 10 so that 1 ml. is equivalent

to 0.01 mg. Pb.

15.   Saturated aqueous solution of sodium pyrophosphate.   This is

rendered lead free by shaking up 100 ml. with 15 ml. ether and

100 mg. sodium diethyldithiocarbamate.

Method.

After shaking the test tube containing the specimen of blood,

20 ml. of its contents are withdrawn in a pipette and mixed with

100 ml. of saturated solution of sodium pyrophosphate in a $4\frac{1}{2}"$ diameter

silica basin (prepared by washing with hot dilute acid and distilled

water).   This is then dried in a hot air oven and is subsequently

ashed over a Bunsen in a fume cupboard.   The presence of excess

phosphate prevents volatilisation of Pb.   After 3 hours ashing the

basin and its contents are cooled and then 1 ml. of conc. HNO_3 carefully

added.   Heating is then continued for a further hour or so.   This

process results in a white ash being formed.

The ash is dissolved by the addition of 5 ml. of conc. HCl in

100 ml. of distilled water and heating over a water bath at $60^{\circ}C$ for

ten minutes.

The dissolved ash is then poured into a 250 ml. separating

funnel into which are also added the washings from the silica basin.

In succession, the following substances are then added into the separating funnel:

1. Ammonia, until the whole solution is alkaline to litmus.   It is then allowed to cool.

2. 5 ml. 20 per cent sodium citrate.

3. 5 ml. 10 per cent KCN.

4. 20 ml. ether.

5. 2 ml. 2 per cent sodium diethyldithiocarbamate.

The separating funnel and its contents are then vigorously shaken.   The ether layer, containing the lead from the ash in the form of an organic complex with sodium diethyldithiocarbamate, separates out.   The aqueous layer is run off, and re-extracted with ether and sodium diethyldithiocarbamate a second time in another separating funnel. The ethereal extracts, after washing with distilled water, are then run into 100 ml. round-bottomed flask, the separating funnels being washed through with 5 ml. ether and this added to the extracts in the flask.

The ethereal solution of lead complex is then put on an electric or steam water bath at 36°C. and the ether evaporated off. The lead complex is stable and remains in the flask.   0.2 ml. concentrated sulphuric acid and 0.5 ml. perchloric acid are then added to the residue, and this is heated over a small flame till the digest is perfectly clear.   After cooling, 3.5 ml. distilled water, 0.2 ml. glacial acetic acid and 1.5 ml. ammonia are added.   The lead has now been changed from an organic into an inorganic state.   The presence of

ammonium acetate ensures that the lead sulphate is in solution (Tompsett,
1939a). 5 ml. of 1 per cent potassium cyanide are then added, and
finally 10 ml. carbon tetrachloride, and the flask and contents well
shaken.

At this stage, the lead standard for colorimetric comparison
is prepared. This is carried out by digesting 1 ml. concentrated
sulphuric acid with 0.5 ml. perchloric acid in 100 ml. round-bottomed
flask over a small flame. When the digest is clear and subsequently
cooled, 18 ml. distilled water, 1.0 ml. glacial acetic acid and 5 ml.
ammonia are, in order, introduced into the flask. Further distilled
water is added to make the total volume up to 25 ml. The mixture is
shaken and 5 ml. are transferred into another 100 ml. flask. A known
amount of Pb. is then added to this (in practice, 0.02 mg. is generally
found suitable, i.e. 2 ml. of the standard solution of Pb. previously
mentioned) followed by 5 ml. 1 per cent potassium cyanide and 10 ml.
carbon tetrachloride.

Subsequently, the treatment of the unknown diluted extract
and a prepared standard of known lead content is exactly the same.
A 1 per cent solution of diphenyldithiocarbazone in carbon tetrachloride
is prepared. This dye, which is green in carbon tetrachloride
solution, is more commonly known as 'dithizone'.   1 ml. of this
solution is shaken up with 10 ml. of 0.5 per cent ammonia. In this
ammoniacal solution dithizone passes into the aqueous phase and
oxidation products remain in the carbon tetrachloride together with a
proportion of unchanged dithizone.

This aqueous ammoniacal solution of dithizone is added
drop by drop to the flasks containing the unknown and standard amounts
of lead till the dye is present in excess. Too great an excess must
be avoided. The correct amount is known when, after shaking, the
carbon tetrachloride has obtained a maximum pink colour caused by the
formation of the lead-dithizone complex, and the supernatant aqueous
layer is tinged with brown.

The contents of the flask are then transferred to 30 ml.
test tubes, and the excess dithizone is removed by washing with aliquots
of 1 per cent potassium cyanide until the aqueous layers are clear. A
pipette attached to a water pump is employed to remove the aqueous
layers. After this process the two test tubes now contain pink lead-
dithizone complex in carbon tetrachloride, each having a volume of 10 ml.
The intensity of pink colour depends on the lead content. Each is
filtered through a Whatman No. 1 filter paper (previously treated with
dilute acid and several changes of distilled water), which removes small
droplets of water remaining in the carbon tetrachloride. The carbon
tetrachloride extracts of unknown and standard are then ready for
colorimetric comparison.

The author has employed a Bausch and Lomb 'Duboscq'
colorimeter. Glass colorimeter cups, kept specially for lead analyses,
are used. The standard is poured in the right hand cup and the unknown
in the left; the standard is set at a depth of 20 on the colorimeter
scale and the unknown matched against it. The reading for the unknown
is noted. This is repeated twice and the average taken. In practice
the pink colours are found easy to match, and the observations always

closely correspond.   Should the unknown be weak the standard may have
to be set at 10 or, if strong, the depth of the standard may have to be
set at 30 or a new standard lead-dithizone complex containing 30 or
40 μg. in 10 ml. carbon tetrachloride made up, put in the right hand cup
and set at a depth of 20 on the colorimeter scale.

The lead content of the unknown is calculated as follows,
the basis of all colorimetry employing the above instrument depending on
the equation:

$$\frac{C_u}{C_k} = \frac{D_k}{D_u}$$

where C_k = Concentration of the known

C_u =   "   " " unknown

D_k = Depth of the known

D_u =   "   "   " unknown

and so:

$$C_u = \frac{C_k \times D_k}{D_u}$$

As a practical example, supposing that 20 ml. of blood
had been ashed and extracted for test as described above, and that a
standard of 0.02 mg. Pb., i.e. 20 μg. (millionths of a gram) had been
employed, then, with a standard set at a depth of 20 on the colorimeter
scale:

$$x = \frac{20 \times 20}{y}$$

where x = concentration of the unknown in μg.
and y = the depth of the unknown.

To express the results in μg. per 100 ml. blood, this result is multiplied by 5. If smaller or larger amounts than 20 ml. blood are ashed, appropriate multiplication by $\frac{100}{z}$ (where z = the number of ml. blood ashed) is carried out. In the author's experience, the use of 20 ml. blood has been found most satisfactory.

The final formula is thus:

$$x = \frac{40,000}{yz}$$

where x = μg. Pb per 100 ml. blood.

y = depth of unknown on the colorimeter scale.

z = number of ml. blood originally ashed, the standard containing 20 μg. Pb set at a depth of 20 on the colorimeter scale.

If, for example, 20 ml. blood had been ashed and, using the above standards of concentration and depth of the known in the colorimeter, the depth of the unknown were 30 on the colorimeter scale, then:

$$x = \frac{40,000}{30 \times 20} = 66.67$$

i.e. the content of lead in the blood tested is 66.7 μg. (recorded as 67 μg.) Pb per 100 ml.

(B) Other biological materials, and water.

The analyses of water, biological tissues and excreta are, in principle, very similar to the method described. Modifications in preparation of the ash and extraction are required, however, when dealing with these and are, briefly, as follows:

Water: A litre of the water to be tested is evaporated to about 100 ml.
Extraction with sodium diethyldithiocarbamate and ether as previously
described is then carried out.   20 ml. of 20 per cent sodium citrate
are employed in this case.   The results are expressed in mg. Pb. per
litre.

Urine: 500 ml. urine are evaporated to dryness in a silica dish in a
hot air oven.   The residue is ashed, and separation and extraction are
carried out as described for blood.   50 ml. of 20 per cent sodium
citrate and 5 ml. of 2 per cent sodium diethyldithiocarbamate are used
in this case.   Digestion with 1 ml. concentrated sulphuric acid and
1 ml. perchloric acid destroys the organic material.   The results are
expressed in mg. Pb. per litre.

Faeces: 10 g. dried faeces are ashed in a silica basin and the contents
dissolved in 100 ml. dilute hydrochloric acid.   The volume is made up
to 200 ml. by the addition of distilled water.   50 ml. of this ash
solution are introduced into a separating funnel, and 10 ml. 2 per cent sod.
diethyldithiocarbamate added.   This is extracted three times with ether,
25 ml. being used on each occasion.   The ether extracts are collected in
a flask and the ether evaporated off over a steam or electric water bath.
The residue is digested with 1 ml. concentrated sulphuric and 1 ml.
perchloric acid.   This is diluted with 20 ml. water, 1 ml. concentrated
hydrochloric acid added and heated to dissolve the digest.   After
rendering ammoniacal as when testing blood, extraction with 5 per cent
sodium diethyldithiocarbamate and ether, with the addition of citrate and

cyanide, is exactly the same as the method previously described in detail. Results are expressed in mg. Pb. in the total daily excretion of faeces.

Bone: 20 g. of fresh bone are ashed in a silica basin. This is treated in the same way as described for faeces. The results are expressed in mg. Pb. per kg. fresh bone.

Soft tissues: 100 ml. saturated solution of sodium pyrophosphate are added to 100 g. of finely divided fresh tissue. After mixing and drying in a hot air oven the material is ashed. After dissolving in 100 ml. water containing 5 ml. concentrated hydrochloric acid the procedure is then the same as for urine. Results are expressed in mg. Pb. per kg. fresh tissue.

Review of the method.

The method can be divided into three stages:

1. The preparation of an ash without loss of Pb. The addition of phosphate to substances of a low phosphate content overcomes this by preventing volatilisation at temperatures below 600°C.

2. Separation of Pb. with ether and sodium diethyldithiocarbamate.

Sodium diethyldithiocarbamate reacts with various metals to form complexes, of which many are soluble in organic solvents. Of those found in water, biological materials and excreta - Fe, Cu, Bi, Zn and Pb form complexes which are soluble in ether. The formation of the Cu and Zn complexes are inhibited if the solution is alkaline and if it contains cyanide. Bismuth complexes may be formed at this stage. The Fe complex does not form if citrate or cyanide is present. In the case of materials

with a high calcium content, precipitates occurring on rendering the
ash solution alkaline make it necessary to carry out a twofold extraction.

3.   The colorimetric estimation of Pb with dithizone.

The extracted lead is converted into the sulphate by
digestion with sulphuric acid and perchloric acid.   An alkaline reaction
(which is formed on the addition of ammonia) is necessary for the
occurrence of the reaction between the lead and the dithizone.   A bismuth-
dithizone complex may also develop at this stage but this is removed by
washing with potassium cyanide, whereas the lead complex is unaffected
by this.

When diphenylthiocarbazone is added, a yellow oxidation
product may pass into the carbon tetrachloride if too great an excess is
added, if the solution is exposed to bright sunlight or if iron or
copper have not been completely removed.

Avoidance of contamination is controlled by the performance
of 'blank' tests - using distilled water instead of blood, excreta or
tissues and treating it in exactly the same way as in the original test.
Although as a rule negative, the occasional finding of a very small amount
of lead (which is so minute as to be beyond accurate comparison even with
very dilute standard) shows the extreme sensitivity of the test.

With care, this difficulty is easily overcome.   Should the
solution not be sufficiently alkaline, a green colour may form in the
carbon tetrachloride.   This is corrected by the further addition of
0.5 per cent ammonia and the subsequent washing with 1 per cent potassium
cyanide.

The author has carried out recovery tests, when certain quantities of lead were added to blood samples of known initial lead content, with satisfactory results. These are recorded in Table II. They are in keeping with the recovery rates of lead found by Tompsett and Anderson (1935) and Tompsett (1936. 1939a) with regard to lead in water, milk, blood and other biological materials.

By this method quantitative estimations of lead can be accurately estimated and fairly easily performed. The method can be learned comparatively quickly, although experience of the technique is needed. Little apparatus is required and large scale purification of reagents is avoided.

Other methods employed for lead analyses.

Although the dithizone method described above was the routine test in the investigations subsequently described, other methods have occasionally been employed.

Methods of water analysis used by Currie (1936) were carried out, with his permission, in the laboratories of the Institute of Hygiene, Glasgow University. These involved the determination of the hardness of water by the soap method, the qualitative testing for lead in water by the bichromate and 'iodide' methods and the quantitative determination of lead by the sulphide method.

Tests for the qualitative estimation of lead in water were performed by boiling down a litre of the water to 200 ml. and then testing the concentrated sample. The presence of lead is indicated by the formation of a yellow precipitate of lead iodide on adding solution of potassium

Table II.

Recovery of lead added to blood.

Initial volume 20 ml.

No.	Initial lead content μ g.	Lead added μ g.	Recovered lead μ g.
1.	28	50	54
2.	28	100	103
3.	28	20	22
4.	28	40	42
5.	28	100	112
6.	7	20	28
7.	24	20	18
8.	24	40	52
9.	24	80	72
10.	15	10	8
11.	18	30	35
12.	11	20	28
15.	11	50	44

iodide. This precipitate dissolves on heating and reappears on cooling. Lead can also be detected by adding potassium bichromate solution to the concentrated sample in a test tube, and noting the development of a yellow colour due to the formation of lead chromate. Control tests employing glass distilled water are carried out at the same time.

These methods, in the author's experience, are of value where the original undiluted sample contains 4 mg. Pb. or more per litre, but are not as a rule sensitive enough when dealing with smaller amounts.

The quantitative determination of lead by the sulphide method is carried out by passing sulphuretted hydrogen from a Kipp generator through 100 ml. concentrated water sample and 3 ml. glacial acetic acid in a Nessler cylinder for three minutes. Brownish-black lead sulphide is formed. A series of standard solutions of lead nitrate in Nessler cylinders, made up with concentrations of 0.1 to 2.0 or more mg. Pb. per 100 ml. are similarly treated, and the unknown is matched against these.

As a practical example, presuming that the unknown matches the tube containing 0.75 mg. Pb. per 100 ml., the unknown would contain the same amount. Therefore 200 ml. (the total concentrated sample) would contain 1.5 mg. Pb. and the undiluted sample of water would contain 7.5 mg. Pb. per litre.

This method, although not so accurate or specific as the dithizone technique, can give very comparable results when testing water containing appreciably large quantities of lead, as is shown

later.   When amounts of lead less than 0.2 mg. per litre are to

be analysed, however, colorimetric estimation employing dithizone

is very much more sensitive and practicable.

(b)   The biochemical behaviour of lead in the body.

The content of lead in blood.

    After absorption, no matter by which route, lead circulates
in the blood stream.   As has already been emphasised, lead absorbed
from the gastro-intestinal tract may not all reach the systemic blood.
Once in the blood, lead can exert its toxic action on the various
systems of the body and can be deposited in different organs and
tissues.

    Opinions differ with regard to the chemical form in which
lead is present in the blood.   Oliver (1914) holds that it is probably
in the form of an albuminate, and Jowett (1932) thinks it forms a
complex inorganic phosphate with calcium and chlorine.   Aub and his
associates (1926) furnished evidence that lead circulates as
colloidal lead hydrogen phosphate ($PbHPO_4$), and Aub published further
results in support of this theory in 1935.   The majority of those
who have studied lead poisoning, including the author, favour this
view although, as has been pointed out by Minot (1938) it is possible
that in such a complex chemical medium as blood lead may be present
in several forms.   The quantity of lead in normal human blood has been
studied by several investigators in the past, and there are considerable
differences in results recorded.   Variations in technique and
geographical distribution may account for this to some extent.

    Table III shows the results of some of these observers,
together with the method employed:

Table III.

Lead content of blood from individuals with no known industrial
exposure to lead.

Author	Method	Range of blood lead values; μg. per 100 ml.	Mean blood lead value; μg. per 100 ml.
Litzner and Weyrauch (1932)	Electrolytic-colorimetric	10-30	-
Litzner and Weyrauch (1933)	Electrolytic-colorimetric	5-50	-
Bass (1933)	Electrolytic-colorimetric	10-50	-
Kehoe, Thamann and Cholak(1933c)	Spectrographic	nil-130	58
Blumberg and Scott (1935)	Spectrographic	5-100	50
Tompsett and Anderson (1935)	Dithizone	40-70	55
Wexler and Sobel (1935)	Spectrographic	less than 100	-
Teisinger (1936)	Micropolarographic	41-79	61
Taeger and Schmitt (1937)	Dithizone	20-60	35
Willoughby and Wilkins (1938)	Dithizone	nil-90	25
Scott and McMillen (1938)	Spectrographic	nil-60	-

Twenty healthy individuals in the Manchester district, and fifty hospital patients in the Glasgow area, all of whom had no known industrial exposure to lead, were tested for the lead content of their blood, by the author, employing the dithizone method. Results are recorded in Tables IV and V.

Table IV.

The blood lead values of normal healthy individuals in the Manchester district.

Test No.	Sex	Age	Occupation	Blood lead μg. per 100 ml.[1]
1	M	18	Laboratory attendant	42
2	M	29	Physician	63
3	M	34	Cabinet maker	87
4	F	27	Secretary	50
5	M	32	Laboratory attendant	71
6	M	26	Chemist	48
7	M	42	Salesman	64
8	M	27	Medical practitioner	69
9	M	27	Pathologist	41
10	M	41	Salesman	72
11	M	24	Salesman	36
12	F	21	Machinist	46
13	M	52	Salesman	47
14	M	31	Warehouseman	67
15	F	25	Bakeress	48
16	M	23	Joiner	88
17	F	21	Waitress	82

Test No.	Sex	Age	Occupation	Blood lead μg. per 100 ml.
18.	M	23	Warehouseman	57
19.	M	36	Salesman	89
20.	F	22	Student	78

Table V.

The blood lead values of 50 hospital patients in the Glasgow area with no known industrial exposure to lead.

Test No.	Sex	Age	Occupation	Disease	Blood lead μg. per 100 ml.
1.	M	30	Motor mechanic	Pleurisy with effusion	48
2.	M	39	Clerk	Pneumothorax	59
3.	F	59	Housewife	Mitral stenosis	35
4.	M	45	Coal miner	Pneumonia (convalescent)	75
5.	M	54	Quartermaster	Nephrosclerosis	47
6.	F	52	Housewife	Mitral incompetence	80
7.	M	24	Lorry driver	Acute nephritis	38
8.	F	39	Housewife	Pneumonia	63
9.	M	21	Pit head worker	Pneumonia (convalescent)	61
10.	F	41	Housewife	Pneumonia (convalescent)	61
11.	M	67	Retired seaman	Myocardial degeneration	66
12.	M	45	Dock labourer	Bronchitis	59
13.	M	49	News reporter	Mitral incompetence	43
14.	F	72	Retired dressmaker	Cerebral thrombosis	56

Test No.	Sex	Age	Occupation	Disease	Blood lead μg. per 100 ml.
15.	M	47	Fitter's helper	Melaena ? cause	40
16.	M	25	Farm labourer	Otitis media	75
17.	F	63	Housewife	Tumour of lung	40
18.	F	69	Housewife	? cholecystitis	76
19.	M	51	Coal miner	Reticulosarcomatosis	55
20.	M	67	Retired fireman	Suppurative arthritis	75
21.	M	48	Milkman	Cardiac decompensation	59
22.	M	23	Coal miner	Pneumonia (convalescent)	40
23.	F	65	Housewife	Erysipelas	40
24.	F	63	Housewife	Diabetes mellitus	45
25.	M	37	Woollen goods factory worker	Duodenal ulcer	59
26.	M	44	Engineer	Aortic aneurysm	49
27.	F	40	Housewife	Pelvic abscess	78
28.	M	46	Clerk	Disseminated sclerosis	30
29.	M	47	Paper mill worker	Erysipelas (convalescent)	68
30.	M	26	Coal miner	Erysipelas (convalescent)	62
31.	M	32	Farm labourer	Essential hypertension	45
32.	M	27	Joiner	Pneumonia (convalescent)	54
33.	M	32	Policeman	Influenza	30
34.	M	54	House furnisher	Erysipelas (convalescent)	74
35.	M	32	Unemployed (ex-plater's helper)	Bronchitis	47

Test No.	Sex	Age	Occupation	Disease	Blood lead µg. per 100 ml.
36.	M	24	Grocer's assistant	Mitral stenosis	65
37.	F	36	Housewife	Renal colic	69
38.	M	37	Clerk	Neurasthenia	43
39.	M	42	Shop assistant	Irido-cyclitis	45
40.	M	52	Machineman	Neoplasm of lung	33
41.	F	18	Domestic servant	Acute rheumatism	44
42.	F	51	Housewife	? cholecystitis	39
43.	M	17	Labourer	Acute rheumatism	41
44.	M	30	Lift erector	Duodenal ulcer	71
45.	M	23	Glazier	Renal glycosuria	55
46.	F	42	Housewife	Subacute rheumatism	68
47.	F	50	Housewife	Multiple neuritis	42
48.	M	61	Clerk of works	Diabetes mellitus	64
49.	F	46	Housewife	Hyperpiesis	48
50.	M	52	Bus driver	Peptic ulcer	55

The lead content of blood in the series of twenty healthy persons living in Manchester was found to have a range of 36 - 89 µg. Pb per 100 ml. with a mean of 62 µg. Pb per 100 ml, while the fifty hospital patients in the Glasgow area had a range of 30 - 80 µg. Pb per 100 ml. with a mean of 54 µg. Pb per 100 ml. The two groups combined gave a mean of 57 µg. Pb per 100 ml., and a histogram of the frequency distributions of blood lead values of these seventy people, with no known industrial exposure to lead is as follows:

CHART 1.
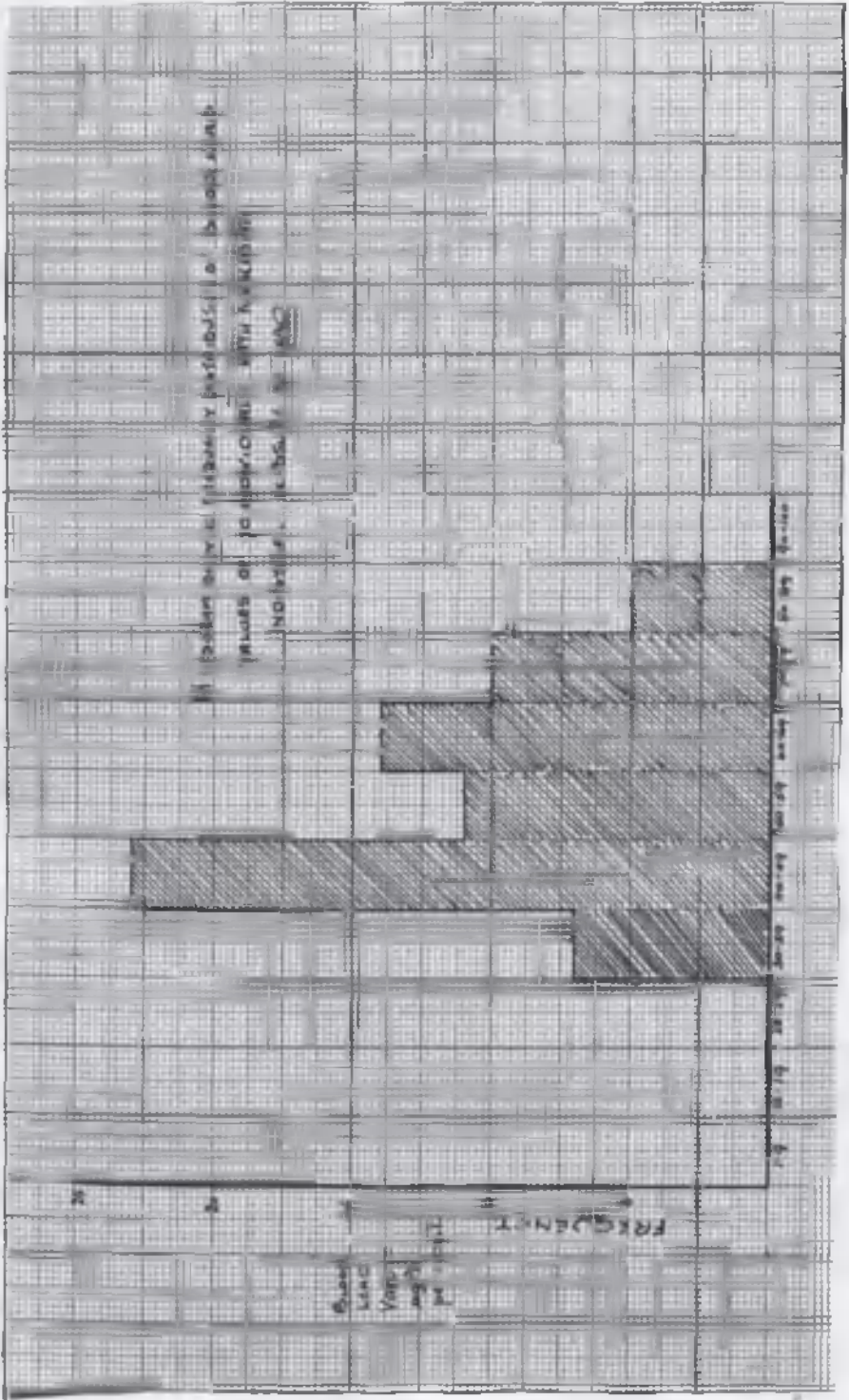
FREQUENCY

It is thus shown that persons with no known industrial exposure to lead may have variable amounts of lead in the blood. Those tested in Manchester, on the whole, showed slightly higher results than the hospital patients in Glasgow, but this difference is negligible.   No connection between age and blood lead value could be made in this series.

The figure of 57μg. Pb per 100 ml. for the mean content of lead in the blood of those not exposed to lead in industry is in close agreement with the findings (see Table II) of Kehoe, Thamann and Cholak (1933c), Tompsett and Anderson (1935) and Teisinger (1936), and the higher figures of the range approximate to those found by Blumberg and Scott (1935), Taeger and Schmitt (1937) and Willoughby and Wilkins (1938).   The results of Litzner and Weyrauch (1932, 1933) are much lower than the author's figures, as are those of Scott and McMillen (1938).

Blumberg and Scott (1935) state that at least 50 per cent, and usually much more, of the lead present in blood is associated with the cells, and they usually found at least 90 per cent in the clot in cases of plumbism, only very minute traces being detected in the plasma.   This is of importance with regard to the excretion of lead, and contradicts the work of Aub (1926) who, employing less sensitive methods, found that most of the lead in blood was in the plasma.

After transportation in the blood, lead is then either stored in the tissues or excreted.

Storage of lead in the body.

It has long been recognised that lead is a cumulative poison in the body (Tanquerel des Planches, 1839), although it was not until the twentieth century that it was more widely realised that lead enters into normal metabolism.

The extensive studies of Aub et alia (1926, 1935) have shown conclusively that the metabolism of lead is closely allied to that of calcium.   The findings of Behrens and Baumann (1933), who ingeniously employed radio-active lead in animal experiments, agree with this. Absorbed lead, which is not excreted, is laid down together with calcium in osseous tissue, the lead hydrogen phosphate circulating in the blood being formed into tri-lead phosphate $(Pb_3(PO_4)_2)$ in the skeleton. This storing of lead in the bones occurs especially in the trabeculae -- the more vascular areas of bone - where, too, calcium derived from the blood stream is also deposited (Bauer, Aub and Albright, 1929).   There is evidence that hard cortical bone also stores lead, but this is a much slower process than in the case of the more vascular portion of the bones.   Distribution of lead throughout the skeleton may be very irregular (Roche Lynch, Slater and Osler, 1934.   Tompsett and Anderson, 1935).

Deposition of lead in the bones is favoured by a high calcium intake, but under certain conditions of metabolic upset - e.g. when a diet poor in calcium is given - the process of lead storage can be reversed and lead again, presumably, as the more soluble salt $PbHPO_4$, re-enters the circulation.   This can also be brought about by the parenteral injection of parathyroid extract ('Parathormone', Lilly) associated with a low calcium intake (Hunter and Aub, 1927).   Under

such conditions calcium is taken from the bones and circulates in
the blood and lead, again following calcium metabolism, likewise re-
enters the blood stream.   The oral administration of drugs which
alter the pH of the blood, especially when the diet is deficient in
calcium, also causes this to occur and ammonium chloride, phosphoric
acid, hydrochloric acid and sodium bicarbonate have been employed to
cause mobilisation of lead from the skeleton.   Potassium iodide,
although its pharmacological action is obscure, has a similar effect
(Aub et al., 1926. Litzner, Weyrauch and Barth, 1931. Tompsett
and Chalmers, 1939).

        After absorption lead can also be deposited in other tissues
such as liver, spleen, kidney, brain and elsewhere.   Such tissues,
obtained at autopsies of those who had no occupational exposure to lead,
were found to contain traces of lead, higher amounts being present in
tissues obtained from individuals who had been exposed to an occupational
lead hazard during life, or who had died of lead poisoning.   The amounts,
however, are by no means comparable with those found in bone.   Traces
of lead have even been found in foetal tissues (Monk, 1933, Tompsett
and Anderson, 1935.   Aub, 1935).

Excretion of lead.

        Although the fact has not long been recognised and still is
not appreciated by many, lead is normally excreted in human faeces and
urine.   It is theoretically possible that it may be excreted through
the skin.

        The work of Kehoe and his associates (1926, 1933a), who found

lead present in the faeces and urine of individuals with no known industrial exposure to lead and even, although the amounts were less, in the excreta of native Mexicans (1933b) was a classical discovery in the field of lead biochemistry.   The source of this lead, as previously described, is mainly dietetic - even under primitive conditions of life.

The amounts of lead in the faeces, which of course include a proportion of unabsorbed lead derived from the diet, are usually higher than the quantities found in urine.   The observation of Blumberg and Scott, previously mentioned concerning the finding of lead in blood cells rather than in the plasma may, in part, account for the larger daily excretion in faeces.   Products of red cells, including lead, broken down in the reticulo-endothelial system in spleen and liver may be excreted in the bile.   Aliavdin and Peregood (1936) found the concentration of lead in duodenal juice to be 10 to 30 times that of the urine.   Their subjects were suffering from lead poisoning, but their analytical results are open to question as they failed to detect any lead in the urine on some occasions.

Under normal conditions of life in America, the mean total daily excretion of lead is approximately 0.3 mg. Pb (Kehoe et al., 1935). Of this 0.06 mg. is excreted in the urine and 0.24 mg. in the faeces. It should be stressed that these are *mean figures*.   The same authorities state that, occasionally, total daily excretion may be 0.36 mg. Pb daily and sometimes more in perfectly healthy individuals with no occupational lead exposure.   This may be due to temporary increases of lead in the diet or to slight metabolic disturbances

which cause mobilisation of lead from the bone trabeculae into the blood stream. There is, however, no close parallelism between blood lead value and the amount excreted (Minot, 1938. Tompsett and Chalmers, 1939). The amounts of lead excreted by persons in Britain closely approximate to Kehoe's figures (Francis, Harvey and Buchan, 1929. Report of Departmental Committee on Ethyl Petrol, 1930. Tompsett and Anderson, 1935).

In general, it may be said that the total lead excretion approximates to the amount ingested daily in the diet, although it frequently is less. The total lead intake includes that absorbed through the respiratory tract derived from atmospheric dust and this, according to the Departmental Committee on Ethyl Petrol may on occasion amount of 0.077 mg. daily, although a proportion of this is again exhaled.

By the fact that storage of lead occurs in the bones, larger quantities being found in the skeleton as age advances (Monier-Williams, 1938), the difference between total daily lead intake and excretion is explained.

AETIOLOGY OF LEAD POISONING AND INCREASED LEAD ABSORPTION.

As mentioned in the introduction of this thesis, lead
poisoning may be of industrial or non-industrial origin.   In both
cases the disease is preventable.

Industrial lead poisoning.

Lead is now encountered in more than two hundred industries
in Britain alone, and thousands of men are employed in factories and
shipyards where they are daily exposed to the risk of increased lead
absorption.   The same occurs in other industrial countries.   While
the total incidence of lead poisoning has fallen enormously it has
been found that in certain trades owing to their expansion and develop-
ment, or to new processes being employed a relatively high number of
cases of plumbism still occur.   Industries such as shipbreaking and
electric accumulator manufacture may be quoted as examples of these.
Table VI shows the distribution of notified cases of lead poisoning
in various industries occurring in Britain in 1900 as compared with
1938.

The most dangerous occupations which have always shown the
highest incidence of lead poisoning are those in which employees are
exposed to lead dust and lead fume.   Under such conditions lead is
inhaled and quickly absorbed in addition to a certain amount being
swallowed.   Lead burners, smelters, pasters and workers in 'lead
stacks' (a process used in the manufacture of lead carbonate) may be
quoted as individuals exposed to this risk.

Table VI.

Notified Cases of Lead Poisoning in Britain.

Industry	1900	1938
Smelting of metals	34[1]	2[1]
Plumbing and soldering	9	2[1]
Shipbreaking	-	13[1]
Printing	18[2]	4[1]
Tinning of metals	5	-
Other contact with molten lead	30[1]	5[1]
White and red lead works	377[6]	9
Pottery	210[8]	3
Vitreous enamelling	11	-
Electric accumulator works	33	10[3]
Paint and colour works	56[1]	8
Indiarubber works	1	-
Coach and car painting	70[5]	1
Shipbuilding	32[2]	5
Paint used in other industries	50[5]	2[1]
Other industries	122[7]	6[1]
Painting of buildings	No figures available	22[7]
Total	1058[38]	96[19]

The principal figures relate to cases and the raised figures to deaths.

A large scale example of risk from lead fume was seen by
the author at the Consolidated Mining and Smelting Company's plant
at Trail, B.C., Canada, where smelting of ore in the form of spelter
was carried out.   In the mining of the ore there was comparatively
little risk, but in the smelting and desilverising processes the danger
from fume was considerable.   In mines where the lead ore is galena
(PbS), there is very little risk of plumbism, but where the ore is
cerussite ($PbCO_3$) miners may suffer from ill-effects, again due to the
inhalation of dust.   Those who handle metallic lead do not run a high
risk of increased absorption, provided that dust and fume (such as
arise in soldering) are avoided.

Carelessness with regard to hygiene on the part of a worker
who allows lead on his person is a further cause of plumbism.   Although
not absorbed through the skin, nail biting, smoking and the taking of
food during working hours or before washing may, in time, result in
relatively large quantities of lead being ingested.   Paint mixing
may be associated with the production of lead dust in the atmosphere
and painters may also be exposed to lead fume when burning off old
paintwork.   Dust may again occur during the process of "dry rubbing
down" (sandpapering painted surfaces) which, although forbidden by the
Lead Paint Regulations (1927), is still practised.

Lack of care when dealing with organic preparations such as
tetra-ethyl lead has on occasions resulted in severe symptoms of
lead intoxication.

Plumbism may also develop in occupations such as pottery,

glazing, the dyeing of yarn with lead chromate, printing with lead-type metal and lead-shot manufacture.

Although the foregoing is a very brief summary regarding the causes of lead poisoning in industry and is by no means complete, it may be said that, in general, any circumstance rendering an employee to be exposed to increased amounts of lead in the atmosphere he works in, or to having lead on his person or clothing may, in time, result in lead poisoning.

Opinions differ as regards the amount of absorbed lead which may give rise to symptoms.   Legge and Goadby (1912) stated that a daily absorption of 2 mg. Pb would in time cause poisoning, and even as recently as 1934 Legge's book, edited by Henry, again mentioned this figure, presumably as a minimum.   Lane (1931) regarded this amount as dangerously high and advocated that there should always be less than 2 mg. Pb per 10 cu. metres of air in the general atmosphere of any factory employing lead processes.   It is extremely difficult to judge a minimum figure as individual tolerance to lead varies enormously, but Lane's standard has given excellent results in practice.

Non-industrial lead poisoning.

Cases of this type of plumbism are now less frequent than in the past.   Water supplies (discussed by Ingleson, 1934), food and food ingredients (reviewed by Monier-Williams, 1938) may give rise to poisoning, as may the wilful taking of lead preparations (Ransome, 1900). 'Accidental' cases, and instances where children have sucked such articles as lead-painted toys have also been reported (Rodgers, Peck and Jupe, 1934).   Gibson (1908, 1931) recorded a most interesting

series of cases occurring amongst children in Australia. Most of them had cerebral symptoms and the cause of their illness was traced to lead carbonate. They had been playing on verandahs, the woodwork of which had been painted with white lead paint; this had dried and flaked due to the action of the sun, the children had got this substance on their hands and had subsequently ingested it. Another strange outbreak of lead poisoning occurred in Baltimore, where a number of families had used discarded battery cases for fuel (Williams et al., 1933). It will thus be seen that non-industrial lead poisoning may arise from very numerous and frequently extremely unusual sources.

Apart from the above, suicidal poisoning by lead has occasionally occurred, but such cases are very rare and as a rule present features distinct from the others under consideration.

THE PATHOLOGY OF LEAD POISONING.

Included under the above heading are the clinical pathology, pathological biochemistry and morbid anatomy associated with increased lead absorption and lead intoxication.

Absorbed lead affects all systems of the body, although one or more may show obvious changes without any gross abnormality being found in the rest.

Haematology.

One of the earliest ill-effects of increased lead absorption falls on the haemopoetic system, anaemia being one of the features in the classical description of the disease. Modern research has shown that the anaemia is caused by lead exerting a toxic action on the erythrocytes in the peripheral circulation, rendering them 'harder' and more resistant to changes of osmotic tension (Aub et al., 1926). They are more brittle and friable than normal cells, due, as it were, to 'lack of elasticity' and are easily damaged and disintegrated. The products of this destruction are taken up by the reticulo-endothelial system and, in this respect, the anaemia is comparable to a 'haemolytic anaemia'. As in such cases, excessive destruction of the erythrocytes in the body in turn leads to an erythroblastic reaction in the bone marrow and this is reflected in the circulating blood by reticulocytosis and the occasional finding of nucleated red cells, which are usually normoblasts.

The view that lead depresses erythropoesis has now for the most part been discarded, although Wilkinson (1936) records lead as a

rare cause of aplastic anaemia, reticulocytosis being absent in such cases. The author has never experienced a case presenting this blood picture, although a macrocytic anaemia with reticulocytosis is recorded in one case of the series subsequently described. A pernicious-like macrocytic anaemia, associated with lead poisoning, has also been described by Davidson et al. (1933). As a general rule, however, the haemoglobin is reduced to a relatively greater extent than the corpuscles and a low colour index results. Very low blood counts are unusual, the red cells rarely being below 2.5 millions per c.mm. There is usually some degree of variation in size and shape of the red cells in the stained blood film. The mean corpuscular volume, according to Whitby and Britton (1937) is low or normal. In relatively acute cases, as in one of the series described later, the van den Bergh is positive, this indicating excessive erythrocyte destruction as already described.

One of the most constant findings in lead poisoning is the presence of stippling of the erythrocytes on examination of the stained blood film. Such stippling, also designated 'punctate basophilia' or 'cells containing Grawitz granules' (after the original observer of this phenomenon associated with lead poisoning (Hawes, 1909)) was for some time regarded as indicative of degenerative changes in the red cells so affected (Ehrlich, 1880). The same interpretation was put on polychromatic cells. Hawes (1909) however, proved that such cells were identical with reticulocytes, and Pappenheim (1914) termed their presence as indicating 'toxic regeneration'. Subsequent experimental work by Key (1924) and Whitby and Britton (1935)

has shown that the stippled and polychromatic cells found in Leishman-stained blood films in lead poisoning are the same as the reticulocytes found on examination of intravitally-stained blood.

Stippled erythrocytes present in blood films stained by Romanowsky dyes, appear as cells containing discrete dots of blue-staining material; the dots are sometimes numerous and granular and sometimes scanty and large. The latter variety as a rule have a greater significance in lead poisoning (Lane, 1931). The cytoplasm of the stippled cell is usually somewhat basophilic. Polychromatic cells appear uniformly stained, being purplish or reddish-blue. In blood films stained by alkaline methylene blue, employing the method subsequently described, normal erythrocytes are stained pale greenish-blue; stippled cells appear bluish with dark blue granules, and polychromatic cells stain a uniform darker blue. This method of staining is more sensitive for the demonstration of stippled and poly-chromatic cells (Whitby and Britton, 1933) as will subsequently be shown, frequently demonstrating their presence in blood films which, if stained by Leishman's method, exhibit no stippling. It is thus important, when recording results, to state the method of staining.

Haematological Technique.

The methods used in the haematological investigations subsequently described were based, with certain modifications, on those advocated by the Standing Committee on Laboratory Methods of the University of Glasgow (1936). Haemoglobin estimations were carried out by Sahli's acid haematin method, and the blood counts performed by

the use of 'Trenner' pipettes and an 'Improved Neubauer' counting chamber. Blood films were made on slides, the blood being spread by using the edge of a second narrower slide to obtain 'margin free' preparations.

Coverslips, prepared with 0.3 per cent alcoholic brilliant cresyl blue and subsequent air-drying, were used for reticulocyte counts. A small drop of blood was 'sandwiched' between two of these prepared coverslips, and, after sliding them apart, the films were counterstained by Leishman's method and mounted in neutral Canada balsam. This procedure obviated making 'wet preparations' which would have been impossible to transport to the laboratory. With the above technique, once the films were made, they could be carried dry and counterstained later.

Leishman's method, and alkaline methylene blue were the two principal methods by which blood films were stained. This latter method (Whitby and Britton, 1933) involves staining with the following alcoholic dye solution:

Methylene blue (Grübler)	1.5 g.
1 per cent potassium alum sulphate in 50 per cent methyl alcohol	0.5 ml.
1 per cent sodium hydroxide in methyl alcohol	0.2 ml.
Methyl alcohol	100 ml.

After staining with the above solution for four seconds the film is rapidly washed with 0.025 per cent sodium hydrogen carbonate in distilled water and dried between layers of filter paper.

For the absolute counts and the examination of stained films a Watson binocular 'Bactil' microscope was employed. In the former case a two third inch objective and x 12 eyepieces were used, and in the latter a combination of a one seventh inch oil immersion objective and x 12 eyepieces or a one twelfth oil immersion objective and x 6 eyepieces.

The stippled cell counts were carried out by the use of modified Ehrlich eyepieces, enumerating and noting the type of these cells present per thousand erythrocytes, and the final result was recorded as 'stippled cells per million erythrocytes'. Various parts of the film were gone over by the 'Meander' method of Schilling (1929), ensuring that as true a representation of the incidence of stippled cells as possible was maintained. Using the above technique there were usually about fifty erythrocytes per field. If stippled cells were numerous two series of a thousand erythrocytes each were examined and the average result recorded. In many cases stippled cells were so infrequent that a count was impossible and these were recorded as being 'very rarely seen, 'occasionally present' or 'a few present' in order as they appeared to the observer. If after an examination of ten minutes no stippled cells had been seen the result was so recorded.

All the haematology was personally conducted, employing standard apparatus, reagents and technique throughout.

<u>The significance of stippled cells. a) In normal blood.</u>

The close correlation between stippled cells, polychromatic cells and reticulocytes is further shown in the present work and it would appear that the granules of the stippled cells are of cytoplasmic origin and a variation of the basophilic substance in the polychromatic staining cells. Both of these types of cell are juvenile erythrocytes, their basophilic properties signifying this (Key, 1921). Whether they appear as polychromatic or as stippled cells varies under different circumstances.

Young red cells are present in normal human blood in numbers usually under 1 per cent of the total erythrocytes, as is shown by the reticulocyte count in health. Blood films from normal individuals stained by Leishman's method show occasional polychromatic cells, these being the same cells as the intravitally stained reticulocytes. Stippled cells have never been seen by the author when this method of staining has been employed. Craik (1937) employing similar staining methods also states that they are never present in health, although Huntington (1939) speaking from a wide experience of practical haematology says that on rare occasions one or two may be seen in healthy blood. When, however, alkaline methylene blue is the staining method employed very finely granular stippled cells can on occasion be seen in normal blood, although a prolonged search is required. They have the appearance of small dots on a background of bluish cell cytoplasm, as if some of the basophilic material of a polychromatic cell had run together into small aggregations. This stippling is finer than that associated with gross disturbance of the

haemopoetic system.

Lane (1931) employing methylene blue staining technique found occasional stippled erythrocytes in about 50 per cent of 223 blood films obtained from a series of students.   While the author agrees that this phenomenon can be met with on rare occasions in apparently healthy blood, appropriately stained, his results show a much lower frequency of occurrence.

A group of 115 healthy individuals in Manchester and Glasgow, composed of medical students, doctors, laboratory workers and blood transfusion volunteers was tested for the presence of stippled cells in blood films, employing the alkaline methylene blue technique. Such cells, usually showing very fine granules, were found in 8 per cent of the films examined.

Thus, from this investigation, finely stippled cells can occasionally be found in apparently normal blood when stained by alkaline methylene blue.   Their occurrence in Leishman stained blood films from healthy persons is doubtful.   In the author's experience they are never found.

b) In diseases other than lead poisoning.

In essential disorders of the blood stippled and polychromatic cells are frequently met with.   Pernicious anaemia, the leukaemias, idiopathic hypochromic anaemia, haemolytic anaemias and acholuric jaundice may be quoted as examples of diseases in which the author has seen this alteration of the erythrocytes.   In all these conditions there are efforts at blood regeneration.

In a series of twenty four cases of pernicious anaemia, haemolytic anaemia and acholuric jaundice the author, employing alkaline methylene blue technique, could demonstrate stippling of the erythrocytes in the peripheral blood in every case although such cells were too infrequent to count with any degree of accuracy. The granules were of small or medium size. Leishman stained films also showed stippling in some of the cases although, as a rule, a longer search was required. All these cases showed reticulocytosis. On the other hand, three cases of aplastic anaemia with erythrocyte counts under a million per c.mm. and, of course, no reticulocytosis, never showed any stippling of the red cells.

c) In lead absorption and lead poisoning.

The mere presence of stippled cells in the blood of a lead worker does not, as will be shown later, signify lead poisoning, but merely indicates his contact with and absorption of lead. The frequency of occurrence of these cells in lead workers varies a great deal. Lane (1931) holds that the presence of stippled cells with small granules up to 3,000 per million erythrocytes is of little or no significance when alkaline methylene blue staining is used. Counts higher than this, more especially if the granules be large, indicate excessive absorption of lead and calls for correction. The author's results are in keeping with this observation.

By this test pre-clinical states of increased lead absorption can be judged and susceptible individuals removed to less hazardous occupations. It is also, if regularly performed, a check on the

suitability of working conditions under which men are employed.

In clinical lead poisoning accompanied by 'classical' symptoms stippling of the erythrocytes is a constant finding in the author's opinion, although the numbers found may vary a great deal in different cases.   They may be as low as 3,500 per million red cells or as high as 56,000 (Leishman).   In less typical cases they may be very infrequent or even absent, this depending on the absolute blood count at the time of test.   Key (1924) found that there was a marked reduction in stippled cells as the total erythrocyte count rose, and the author's findings are in keeping with this observation. The number of stippled cells also declines or disappears - sometimes rapidly - after cessation of exposure to lead (Brookfield, 1928. Lane, 1931) and this has to be borne in mind when lead has caused organic changes in other systems.   Some chronic cases, especially when they have a persistent anaemia, however, have stippled cells in their blood for years.

The discovery of such cells in blood films of those with no occupational exposure to lead should always cause increased lead absorption to be considered in the differential diagnosis, bearing in mind the other conditions, previously mentioned, in which stippling may be encountered.   This finding was the first clue to an outbreak of non-industrial lead poisoning described in a later section of this work.   Compared with its occurrence in other diseases a far higher number of stippled cells is met with in increased lead absorption and lead poisoning.   In the former polychromatic cells far outnumber

those which are stippled, whereas in the latter both these types of cell are more evenly distributed and the granules of the stippled cells are larger.

The nature of the granules in stippled cells.

Much discussion has taken place regarding the causation of stippling of the erythrocytes. Some authorities (Piney, 1932) regard the granules as being nuclear remnants derived from the nuclei of normoblasts, but this is probably not the case, as Brookfield (1928) quotes Grawitz as finding the granules transparent to ultra violet light, whereas nuclear material was opaque and the author has frequently seen stippled normoblasts with nuclei perfectly intact. In vitro experiments failed to show that the direct action of lead on red cells accounts for the stippling (Aub et al., 1926). Brookfield found that, when using intra-vital staining the reticular substance of juvenile red cells could be changed to dots resembling stippled cells by altering the strength of the cresyl blue, and while the author agrees that the variation in staining technique plays a very important part in whether a cell shows as stippled or polychromatic, he, however, designates all intra-vitally stained cells as reticulocytes.

As already stated, when stippled and polychromatic cells are found, there is also reticulocytosis, and so the latter is a more delicate although very much less specific test for increased lead absorption than is a stippled cell count. The nature of the reticular substance in intra-vitally stained young red cells is also obscure - it is certainly not of nuclear origin as the author has seen reticulated normoblasts in many disorders of the blood - and it would appear that

this change as well as stippling is a staining reaction due to some alteration of the basophilic substance in the cytoplasm of poly-chromatic cells caused by lead or by some other means (Whitby and Britton, 1933). The exact nature is unknown.

The effect of lead on leucocytes.

In clinical lead poisoning there is as a rule little change in the leucocyte count, although in the series of cases examined by the author slight increase of lymphocytes and monocytes in the differential count was occasionally noticed. This was by no means constant. Ferguson and Ferguson (1934) and Shiels (1936) have stressed the value of the lymphocytic ratio:

$$\frac{\text{large lymphocytes} + \text{monocytes}}{\text{small lymphocytes}}$$

as a prognostic sign in persons exposed to lead. An increase in the ratio is said to occur early in exposure and later falls markedly as symptoms develop.

In experimental lead poisoning in animals Brockfield (1928) occasionally noted a leucocytosis affecting the granulocytes, and Blair Bell (1930) occasionally noted a similar occurrence in cases of cancer treated with intravenous colloidal lead, but clinically leucocytosis is usually absent. The author has only once seen a mild polymorphonuclear leucocytosis associated with lead colic. This absence of leucocytosis is an important point in differentiating lead poisoning from inflammatory abdominal conditions.

Pathological biochemistry.

Lead in excreta.

As long ago as 1883 Putnam described cases of plumbism where lead was found 'in considerable amounts' in the urine. As a result of improved laboratory methods and the recognition of the importance of faecal excretion various 'pathological levels' of lead excretion have been suggested (Tompsett and Anderson, 1939). Kehoe et al. (1933), however, found that just as in the 'unexposed population', lead excretion varies greatly in healthy lead workers. Bearing in mind the numerous factors already mentioned concerned with lead excretion, this is not surprising.

Urine: Men exposed to the lead hazard in industry were found to excrete an average of 0.3 mg. Pb per litre in the urine; occasionally figures up to nearly 1.0 mg. Pb per litre were met with (Departmental Committee on Ethyl Petrol Final Report, 1930). Lewis (1932) recorded figures up to 1.89 mg. Pb per litre in workers not showing any toxic effects. Kehoe and his associates (1933) found amounts up to 0.34 mg. Pb per litre in a large group of asymptomatic lead workers, and states that the mean daily urinary lead excretion of lead workers is about 0.2 mg. Cases suffering from lead poisoning may have more than this in the urine but frequently the amount is less and may be within the limits of normal (Monier-Williams, 1938). Dietetic and metabolic variations account for this

and any result recorded should be interpreted together with consideration
of the patient's diet and condition (e.g. renal function) at the time
of test.   The varying results regarding the urinary content of lead
by certain investigators (e.g. Lewis) may be due in part to such
influences.

Faeces: The importance of excretion of lead in the faeces was not
fully recognised till relatively recently (Aub et al., 1926).   Amounts
of lead over 0.6 mg. per sample (i.e. one complete bowel motion),
according to Kehoe indicate high exposure to lead, and amounts up to
7.6 mg. Pb per sample may be found in apparently healthy lead workers.
Such high figures however, if maintained, are associated with impending
clinical plumbism.   Testing a large series of asymptomatic lead
workers he found that the average amount of lead per sample of faeces
was 2.0 mg.   Clinical lead poisoning had, however, developed on
certain occasions in men working under the same conditions. As a
general rule, the daily excretion of 1 mg. Pb or more occurs in
association with clinical plumbism, but factors such as diet may cause
the results to be very variable, as has been found by the author and
other observers.

Total excretion: The sum of the urinary and faecal excretion per
day is generally regarded as being the total daily excretion of lead.
Although Melnick and Cowgill (1935) found increased amounts of lead
in hair in a small series of lead workers, this method of excretion
seems relatively unimportant, and contamination is unavoidable.

          Tompsett and Anderson (1939) regard a daily excretion of
over 1 mg. a day to be indicative of lead poisoning.   This view, in

the author's opinion, should be taken with reserve on account of the
great variations in excretion which may occur in healthy lead workers.
Evidence of high excretion, however, may be of great value when taken
into consideration with other data.   Kehoe regards a total excretion
of 1.1 mg. Pb a day as indicating excessive absorption which, in time,
might give rise to lead poisoning.   He does not regard it as proof
of the disease.

Blood.

As the toxic action of lead depends on that amount circulating
in the blood stream estimation of the lead content of the blood serves
as a valuable guide to detection of increased lead absorption.   The
upper limits of normal vary according to different observers.   Litzner
and Weyrauch (1933) regarded $60\,\mu g$. Pb per 100 ml. as the level at
which symptoms may be expected, while Teisinger (1936), Taeger and
Schmitt (1937) and Tompsett and Anderson have put down $100\,\mu g$. Pb
per 100 ml. as the level above which symptoms of lead poisoning
develop.   Blumberg and Scott (1935) consider 100-$200\,\mu g$. Pb per 100
ml. as the 'critical range'.

The author personally interviewed and tested a series of
forty four lead workers in various trades who were all in good health
and regularly seen by examining surgeons under the Factories Act.
Their blood lead values are recorded in Table VII.   Each man had a
haemoglobin estimation performed and an examination for stippled cells.
A reticulocyte count was also carried out.   Notes regarding duration
of exposure to lead, personal habits, general condition of health and
the state of the gums are also included.

TABLE VII.

Case No.	Duration of exposure in yrs.	Age	Hb. per cent.	Leishman film	Methyl blue film	Ratio count %	Blood lead μg. per 100 ml.	Notes.
1.	5½	32	92	No stippling.	Very occasional stippling and polychromes.	1.25	80	Always healthy. Total abstainer. Milk: 2 pints daily. False teeth.
2.	One month	28	95	No stippling. Normochromic.	Two stippled and a few poly-chromes in whole exam.	1	99	Hands and nails very dirty. Only a month in this job - was previously a bricklayer. Teeth good. No complaints or signs.
3.	5½	50	92	A few stippled cells seen (small and medium). Also polychromes.		2.25	118	Healthy. 1 pint of milk a day. Beer and spirits at weekends. No complaints or signs.
4.	4⅓	58	96	Normochromic. Very occasional S. and P.	Very few S. - more than Leishman.	1.25	125	Slight exophthalmos. Artificial teeth. Takes a lot of milk. Nervous. Beer and spirits at weekends - never to excess.
5.	27	45	98	Nil abnormal.	No stippling. Scanty poly-chromes.	$>$ 1	72	Mixing white lead in oil. Had worked in 'lead stack'. False teeth. Said to have had blue line 5 years previously. Looks pale. Clinically healthy. Pint of milk daily - hardly any alcohol.

Case No.	Duration of exposure in yrs.	Age	Hb. per cent.	Leishman film	Methyl blue film	Retic count %	Blood lead µg. per 100 ml.	Notes.
6.	3 weeks	25	90	Nil abnormal.	Scanty stippling. 1 Stipples small and medium. A few polychromes.	1	70	High exposure to lead absorption. Wears respirator. Works in 'lead stacks' - white lead one week and metallic lead the next. Dust +. Clinically healthy. Several carious teeth; no line. Always good health. Odd beer at weekends. ½ pint of milk daily.
7.	20	35	85	Normochromic. A very few stippled and polychromes (small and medium).	Scanty stippled and polychromes. (More than Leishman).	1.25	93	Edentulous. Looks pale. Never symptoms. Drinks 2 pints of milk a day. Temperate.
8.	5	31	88	Normochromic. Very few S. and P. (Small and medium).	Very few S. and P. (small and Medium).	1.5	118	Lead smelter - always good health. Good physique. False teeth. Milk - over a pint a day. Occasional alcohol.
9.	8	36	94	Normal. No stippling.	No stippling.	> 1	125	Scrap lead worker. Always excellent health. Good teeth; gums normal. Total abstainer.
10.	44	61	87	Normal. No stippling.	No stippling.	> 1	75	Total abstainer. Milk +++ in diet. False teeth. 'Thought he had colic 13 years ago'—never off work. Looks healthy and active.

Case No.	Duration of exposure in yrs.	Age	Hb. per cent.	Leishman film	Methyl blue film	Retic count %	Blood lead μg. per 100 ml.	Notes.
11.	3	32	88	Normochromic. Very few stippled and polychromes.	A very few stippled and polychromes (more than Leishman).	1.75	107	Always healthy. Good teeth. Gums normal. Never alcohol to excess. Regular, large amounts of milk daily.
12.	24	50	75	Somewhat hypochromic. A few S. and P. (medium and small).	S. and P. more frequent than in Leishman film (small, medium and large).	2.0	134	Brass and lead worker (dust). Looks pale. No complaints, but said he had lead colic 10 years ago. Milk nil.
13.	3	30	95	Normochromic. Occasional P. but no stippled cells.	No stippled cells seen.	1.5	96	Lead alloy worker. Looks a bit pale. Good build. Always good health. False teeth. Alcohol occasionally.
14.	4	29	92	Normochromic. Few S. and P.	Few S. and P. (more than Leishman).	3.0	85	Always healthy. Good physique. False teeth. Alcohol - not excessive.
15.	3½	28	100	Nil abnormal.	Very scanty stippled cells (small), and polychromes.	1	122	'Lead stacks' worker. High exposure. Clinical condition very good. Good teeth. Athletic. ½ pint of milk daily. Good deal of beer and spirits at weekends.

Case No.	Duration of exposure in yrs.	Age	Hb. per cent.	Leishman film	Methyl blue film	Retic count %	Blood lead µg. per 100 ml.	Notes.
16.	13	57	95	Nil abnormal.	Very occasional stippled cells (small) and few polychromes.	1	165	Lead casting. Some fume, but effective local exhaust. Large muscular build. Slight (definite) blue line on gums. Some carious teeth. General condition very good. Asymptomatic. Milk - ½ pint or so a day. Moderate amount of alcohol at weekends.
17.	7	43	95	Nil abnormal.	Very scanty stippling (small) and polychromes.	>1	52	Always been healthy. Some carious teeth. Clinically sound. Never has complaints. Takes ½ pint of milk daily; only very occasional alcohol. Works in lead grinding department (wet methods used).
18.	8 months	24	90	Very few stippled cells (small and medium) and polychromes.	Stippled cells more frequent than in Leishman film (small and medium). A few polychromes.	1.75	115	Always good general health. Edentulous. Clinically: looks pale, but mucous membranes well coloured. Rather thin subject. Asymptomatic. Takes ½ pint of milk daily. Only very occasional alcohol. Works in lead stacks.

Case No.	Duration of exposure in yrs.	Age	Hb. per cent.	Leishman film	Methyl blue film	Retic count	Blood lead μg. per 100 ml.	Notes.
19.	4½	27	80	Obvious stippling, although too few to count (small and medium).	Stippled (large, medium and small): 1 per 1,500. Polychromes: 1 per 200.	3	129	Works in lead stacks. Never complained. Clinically sound, although looks rather pale. Mucous membranes satisfactory. There is a slight but definite blue line on the gums. A few teeth carious. Milk – ½ pint or so daily. Beer (moderate) at weekends.
20.	40	55	88	Nil abnormal.	A few poly-chromes but no stippling.	>1	115	General work in lead works. Mostly administrative. Used to work in stacks and grinding. Clinically satisfactory. Edentulous. No complaints at any time. Pint of milk a day. Very occasional alcohol (beer and spirits).
21.	1	44	90	Nil abnormal.	Very few polychromes and an occasional stippled cell (small).	1.5	119	Works in lead stacks. Clinically satisfactory; teeth good. Never any symptoms. Doesn't take much milk. Beer and spirits at weekends only.

Case No.	Duration of exposure in yrs.	Age	Hb. per cent.	Leishman film	Methyl blue film	Retic count %	Blood lead µg. per 100 ml.	Notes.
22.	5½	27	80	A few poly-chromes. Occasional finely stippled cells. A hypo-chromic picture.	Stippled cells (large, medium and small) stippled fairly frequent. Fairly frequent polychromes.	2.5	152	No symptoms. Works in lead stacks. Looks pale; rather thin. Good teeth. Takes milk but not regularly. Total abstainer.
23.	27	45	100	Nil abnormal.	Very occasional stippling and polychromasia.	1	106	Works foreman. General duties. Sometimes exposed to dust, but not so much as previously, when working in stacks and grinding. Clinically satisfactory. Never any complaints. Teeth good. Occasional alcohol, but never excessive. Takes one pint of milk a day.
24.	4	28	100	Nil abnormal.	Very occasional stippling (small and medium) and polychromes.	>1	85	Red lead furnace worker. Moderate exposure. Looks rather pale, but general condition good. Most of teeth extracted, but several carious stumps. Never any symptoms. Doesn't take much milk. Beer: 2-3 pints at weekends.

Case No.	Duration of exposure in yrs.	Age	Hb. per cent.	Leishman film	Methyl blue film	Ratio count	Blood lead µg. per 100ml.	Notes.
25.	One month	32	80	Occasional polychromes. No stippling. Normochromic.	Very occasional finely stippled cells and poly-chromes.	1.5	65	Working mixing white lead and oil. Low exposure and only for a week. No symptoms and previous health always good. Had been a farm labourer. Colour good and general examination satisfactory. Teeth good. Takes a good deal of milk – a pint or more daily. Occasionally takes 1-2 pints of beer at weekends.
26.	1	50	100	Normochromic. Very occasional polychromes and stippled cells (small and medium). Not estimable.	A few stippled cells (small and medium). More than Leishman, but very infrequent.	1	119	Works in lead stacks. Colour rather poor, but mucous membranes good. Never any symptoms. General examination satisfactory. Doesn't take much milk. 1-2 pints of beer at weekends.
27.	14	55	100	Normal film. No stippling seen.	Very occasional finely stippled cells.	>1	64	Lead paint works labourer. Low exposure, although some dust at times. General condition satisfactory. No history of symptoms. Several carious teeth. Takes 1-2 pints milk daily. Beer (2-4) pints at weekends.

Case No.	Duration of exposure in yrs.	Age	Hb. per cent.	Leishman film	Methyl blue film	Retic count	Blood lead µg. per 100 ml.	Notes.
28.	12	53	95	Normal film. No stippling seen.	A very occasional stippled cell.	1	92	Smelting pot - metallic lead. Some fume, but efficient local exhaust ventilation. Clinically satisfactory. No symptoms. False teeth. ½ pint of milk daily. Beer at weekends occasionally.
29.	20	50	95	Normal film. No stippling seen.	No stippled cells seen.	>1	121	Good colour. Teeth and gums healthy. Clinically satisfactory. Doesn't take much milk. Moderate beer and spirits at weekends.
30.	Ten days	29	96	Normal film. No stippling.	No stippled cells seen.	>1	81	Slight exposure. Previously farm worker. Always healthy. Clinically satisfactory. Moderate colour of skin, and mucous membranes well-coloured. Artificial teeth. 1 pint or more of milk a day. Very occasional beer.
31.	18	44	98	Normal film. No stippling seen.	No stippled cells seen.	>1	64	Dry colours. Clinically satisfactory; good colour. A few carious teeth. Never any symptoms. Takes very little milk. Occasional beer at weekends.

Case No.	Duration of exposure in yrs.	Age	Hb. per cent.	Leishman film	Methyl blue film	Retic count	Blood lead μg. per 100 ml.	Notes.
32.	1	51	89	Nil abnormal.	A very few stippled cells (small and medium).	1.5	109	Works in lead stacks. Clinically satisfactory; looks rather pale, however, but never any history of symptoms. A few carious teeth, also a faint blue line – irregular. Milk: approximately ½ pint daily. Moderate beer and spirits at weekends.
33.	31	55	95	Very scanty stippled cells and polychromes.	Very few stippled (medium and small) and polychromes.	1.75	119	Working at white lead and oil mixing. Had previously worked in stacks. A thin but healthy man. No history of symptoms apart from occasional diarrhoea. Milk: takes very little. Alcohol regularly.
34.	29	51	75	Very occasional stippling (medium and small) and polychromes.	An occasional stippled cell seen.	2.0	108	At present yard foreman. Previously worked in stacks and at grinding. A thin, pale man. Never complained at all. Does not look very healthy. Teeth dirty and carious. Does not take much milk. Alcohol-a good deal of spirits and beer at the weekends.

Case No.	Duration of exposure in yrs.	Age	Hb. per cent.	Leishman film	Methyl blue film	Retic count %	Blood lead μg. per 100 ml.	Notes.
35.	28	59	90	Nil abnormal.	Very occasional stippling and polychromasia.	1	95	General duties in lead works. Not much exposed now, but used to be grinding. No history of symptoms. Clinically satisfactory. Teeth carious and a tinge of 'blue line'. Takes a good deal of alcohol (beer and spirits) regularly. Only occasional milk.
36.	14	32	94	Normal film. No stippling seen.	No stippling seen.	>1	70	Scraping casks which contained white lead. Teeth: upper false, others fair. General condition satisfactory. Never any symptoms. Takes a little milk. 1-2 pints of beer at weekends.
37.	5	21	100	Normal film.	A very occasional finely stippled cell seen.	1.25	75	Scraping white lead (casks). Colour good. Teeth: several carious stumps. General condition very good. Never any symptoms. Doesn't take much milk. Occasional ½ pint of beer.

Case No.	Duration of exposure in yrs.	Age	Hb. per cent.	Leishman film	Methyl blue film	Ratio count %	Blood lead μ g. per 100 ml.	Notes.
58.	20	49	100	Very occasional finely stippled cells and poly-chromes.	A very few stippled and polychromatic cells.	1	108	Putty maker. Good colour. Artificial teeth. General condition very good. Asymptomatic. Takes very little milk. Total abstainer.
39.	14	44	86	Very occasional polychromes. No stippling. Normochromic.	Occasional polychromes. No stippling.	> 1	86	No history of past illness. Worked as accumulator paster for 14 years. Never shown symptoms of excessive lead absorption. Never had raised punctate count, nor fall in Hb. Work has definitely high lead hazard. Takes ½ pint of milk daily; 12 pints of beer at weekend.
40.	13	37	90	Very occasional polychromes and few stippled cells (small). Normochromic.	A very few stippled cells and poly-chromes.	1.75	166	Worked for 13 years in Pasting Dept. Risk as Case 39. Nothing notable in previous medical history. Takes 2 pints of milk a day. Almost no alcohol (an odd half pint).

Case No.	Duration of exposure in yrs.	Age	Hb. per cent.	Leishman film	Methyl blue film	Retic count %	Blood lead μg. per 100 ml.	Notes.
41.	15	45	79	Normal film. No polychromes or stippled cells seen.	A very few stippled and polychromatic cells.	1.25	149	Lead pasting. On several occasions in past had shown high punctate counts. ½ pint of milk a day. Beer – 2 pints a day.
42.	13	36	90	An odd poly-chrome. No stippling. Normochromic.	Very occasional polychromes, but no stippling.	>1	96	Paster. No history of past illness. Never shown an increased polychrome count, or lowered Hb. Takes one pint of milk a day. Practically no alcohol.
43.		42	91	Normal film. No stippling or polychromes.	A very occasional stippled cell and scanty polychromes.	1	60	No history of previous illness. Works in red lead filling dept. Alternate 4 weeks at this and a non-hazardous dept. Wears respirators and complete change of clothing. With this, less risk than in pasting dept. Not shown raised punctate count for 5 years. ½ pint of milk and one pint beer per day.

Case No.	Duration of exposure in yrs.	Age	Hb. per cent.	Leishman film	Methyl blue film	Ratio count %	Blood lead μg. per 100 ml.	Notes.
44.	25	51	96	A very few polychromes and scanty stippled cells	Scanty stippling (small) and very occasional polychromes.	1.75	192	Worked for 25 years in red lead filling dept. In past very dangerous work, but conditions improved in last 9 years, as mentioned in case 43. Worked as inspector and charge hand, not being subject to monthly changes. Probably in past, more heavily leaded than any other employee. Takes one pint of milk a day and an odd half pint of beer.

In this series:

Blood lead levels ranged from 52 - 192 μg. Pb per 100 ml., with a mean of 104 μg. per 100 ml.

Haemoglobin levels ranged from 75 to 100 per cent, with a mean of 91 per cent.

14, or 32 per cent showed stippled red cells when stained by Leishman's method.

34, or 77 per cent showed stippled red cells when stained by the alkaline methylene blue method.

In no case were stippled cells so frequent as to be counted with any attempt at accuracy.

Reticulocytes were never more than 3 per cent.

These men, all with definite daily exposure to lead
during the course of their work were found to have lead in their blood
ranging from 52 μg. (within the author's "normal limits") to 192 μg.
per 100 ml.   The mean value was 104 μg. per 100 ml. and their frequency
distribution is seen in Chart 2 .

Twenty three of them (55 per cent) had blood lead values
over 100 μg. per 100 ml. - the so-called limiting value of certain
other workers.   Just as the normal blood lead value is a range, so
there is a range in lead workers, and the author considers that figures
of over 100 μg. Pb per 100 ml., although indicating increased
absorption, do not of necessity indicate lead intoxication.   As has
already been pointed out (Tompsett and Chalmers, 1939), factors such
as diet play an important part in relationship to the blood lead value
at any given time, and moreover, individual tolerance to lead varies
a great deal (Oliver, 1914).   Kehoe and his colleagues (1933c) also
refrained from stating a critical level of blood lead value, and record
typical cases of lead poisoning with less than 100 μg. Pb per 100 ml.
of blood.   Similar cases have been reported by Taeger and Schmitt
(1937), and by the author in the present work.   No correlation between
the content of lead in the blood and that in the excreta has been found
(Kehoe, 1933c. Taeger and Schmitt, 1937. Tompsett and Anderson,
1939). As a general rule, however, the blood lead content is definitely
raised in clinical lead poisoning, and values ranging from 100 μg.
up to 500 μg. and more have been recorded, (Kehoe et al. (1933c)
Taeger and Schmitt, 1937.   Chalmers and Tompsett, 1938.   Tompsett
and Anderson, 1939.   Tompsett and Chalmers, 1939).
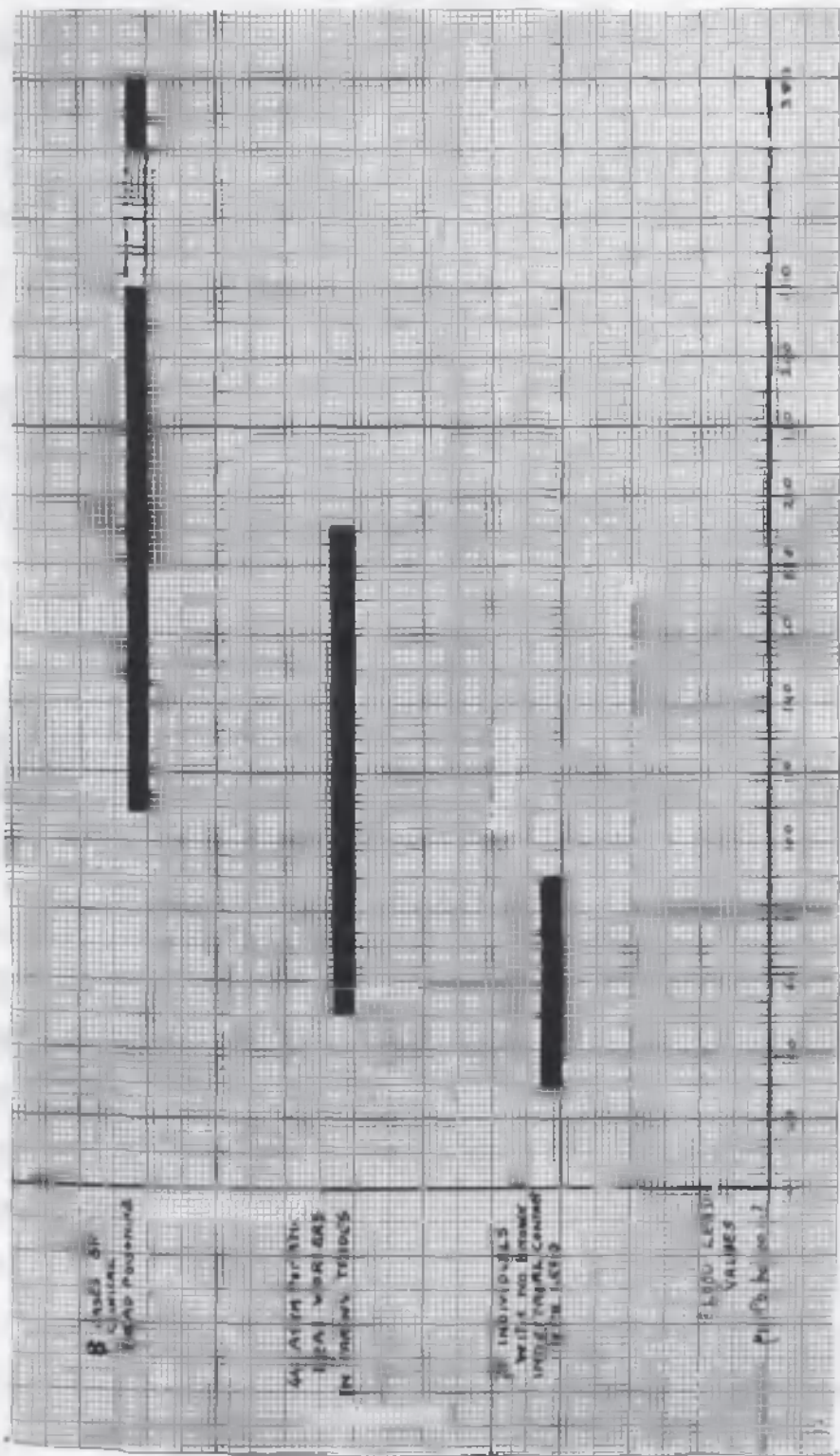
CHART 2.
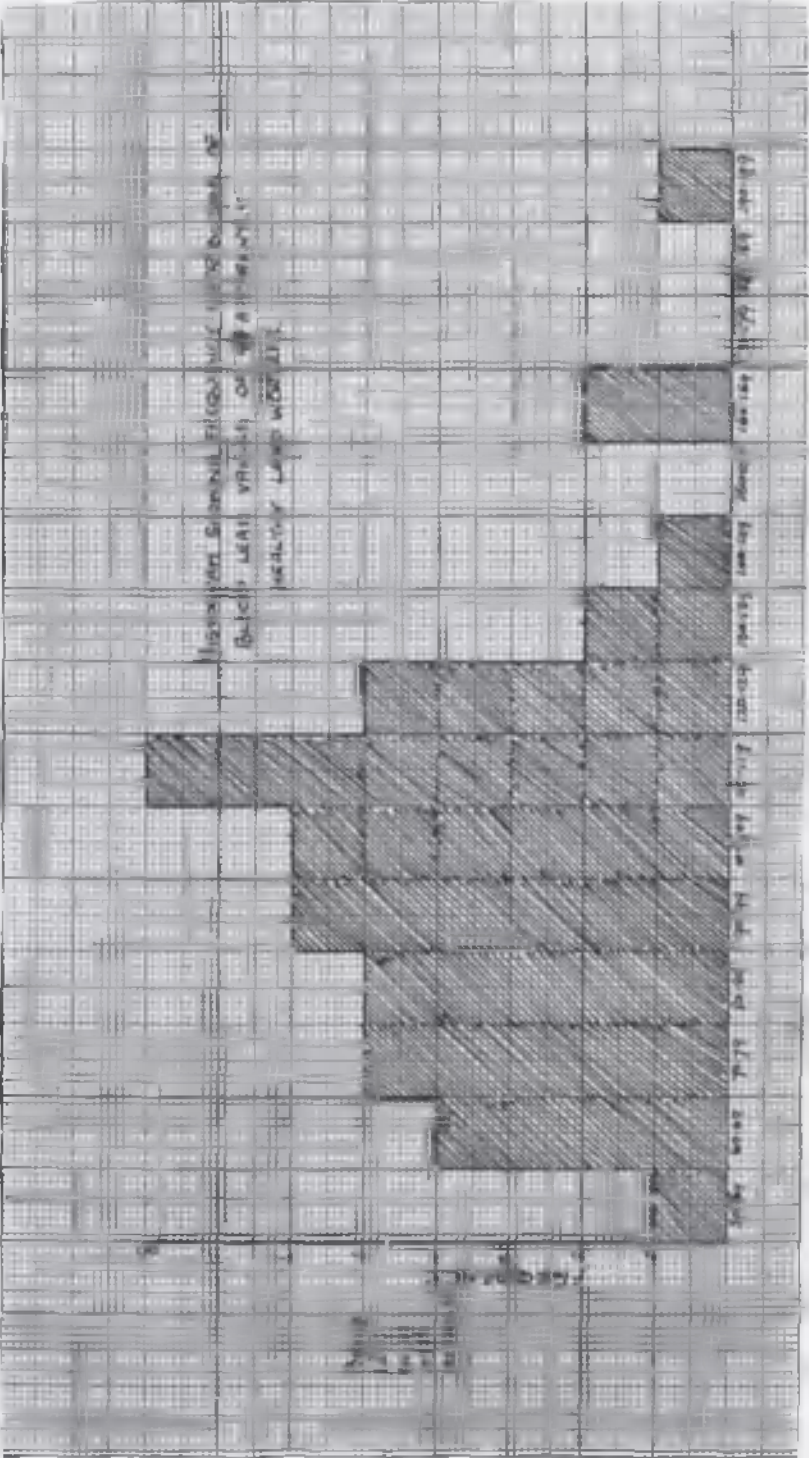
According to the author, there is thus no threshold
of blood lead value at which symptoms appear, the normal range,
the range found in lead workers and those values found in clinical
plumbism all tending to overlap each other, as is shown in Chart 3.

Tissues.

Chemical analysis of tissues obtained at autopsy of those
who have died from lead poisoning or who have been exposed to high
'lead risk' during life show an increase in the lead content of most
of the tissues (Aub et al., 1926.   Lynch, Slater and Osler, 1934.
Tompsett and Anderson, 1935), the highest amounts being found in the
skeleton.   Liver, spleen, and kidney may also show considerably
increased amounts of lead on occasion and in the present work a woman
dying from lead encephalopathy was found to have six times the normal
amount of lead in the brain.   Blair Bell (1930) found lead, after
its intravenous injection, to be present in high amounts in cancerous
tissues and in the cells of the reticulo-endothelial system, the bones
containing comparatively small amounts.   The majority of workers,
however, agree that the highest amounts are usually detected in the
bones, especially more vascular bones such as ribs and vertebrae,
although long bones such as the tibia and femur may also show a con-
siderable increase (Tompsett, 1936).

Such findings do not by any means constitute proof of the cause
of death being lead poisoning, but may furnish valuable information as
to there having been increased exposure during life.

CHART 3.

B CASES OF CLINICAL LEAD POISONING

A. AT 37 PERSONS IN A WORKS IN FAIRVIEW TERRACE

P INDIVIDUALS WITH NO EVIDENCE UNDER NORMAL CONDITIONS (1910-1922)

BLOOD LEAD VALUES
PER 100 ML.

Morbid anatomy of increased lead absorption and lead poisoning.

The lead line in the gums is present only in subjects with teeth. The bluish black colour is apparently due to lead sulphide formed by the interaction of lead and sulphuretted hydrogen derived from putrefaction in the mouth. Microscopical examination shows the 'line' to be made up of numerous small dots of sulphide of lead and the deposit lies in the gingiva, slightly away from its margin, and cannot be rubbed off. It is most obvious close to the bases of carious teeth. Blue discoloration of similar origin has also been described as occurring on the mucosa of the mouth and large intestine (Oliver, 1914. Legge, 1934).

As a general rule, the body shows loss of subcutaneous fat and generalised pallor of the tissues. This was first noted by Laenneo (1831). The bone marrow is frequently hyperplastic in relatively acute cases.

Lead has been regarded as the cause of numerous morbid changes in the body. Most authorities regard granular contraction of the kidneys, arteriosclerosis and associated enlargement of the heart to be one of the most constant findings in chronic cases. Lead apparently acts as a mild irritant to the kidney and its vessels (Muir, 1933). The importance of lead as a cause of chronic nephritis in young adults has been stressed by Nye (1933) working in Queensland. Some cases of lead poisoning, such as that subsequently quoted by the author, show very little evidence of kidney damage at post mortem. Many of the other cases showed no obvious clinical signs of renal insufficiency. Jones (1935) found no greater incidence of arterio-

sclerosis and renal disease in a group of heavily exposed lead workers than in a control series of men with no occupational lead hazard.

Colic has been attributed to sclerosis of the coeliac ganglion of the sympathic nervous system, and Legge and Goadby (1912) noted degeneration of the muscular coats of the stomach and small intestine, accompanied by infiltration and small haemorrhages.

In cases of lead encephalopathy, changes in the brain such as hardness and flattening of the convolutions (Oliver, 1914), degeneration of cortical cells, small haemorrhages, meningeal thickening (Legge, 1933) and round celled infiltration have been described. None of them are constant. In cases where there has been paralysis of the limbs, degeneration of peripheral nerves and on occasion associated muscular atrophy have been found. Degeneration of the anterior horn cells of the spinal cord is as a rule a later development than the peripheral neuritis. Patches of sclerosis in the cord have also been described (Kinnear Wilson, 1907). Among other changes which have on occasion been regarded as due to the action of lead may be mentioned gastric ulceration (Lewis, 1932), optic atrophy and neuro-retinitis, vascular haemorrhages, degeneration and cirrhosis of the liver and excess of pigment in the reticulo-endothelial system. Blackman (1936) described 'inclusion bodies' present in the cells of kidney, liver, bone-marrow and spleen.

The above description includes some only of the very numerous

morbid changes which have been attributed to lead.   Apart from the

lead line on the gums none of them can be regarded as typical of

increased lead absorption or lead poisoning.

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SYMPTOMS, CLINICAL FINDINGS AND DIAGNOSIS OF LEAD POISONING.

Although plumbism is at times regarded as being either
acute or chronic there is no sharp dividing line between the two
conditions as, apart from rare 'suicidal' cases where the symptoms
are those of severe gastro-intestinal irritation, the clinical picture
of the relatively acute case closely simulates that of the 'toxic
episodes' of the chronic form of the disease.   The acute cerebral
symptoms associated with tetra-ethyl lead poisoning are, however,
an exception.

Sex and age incidence: The disease may develop at any age, although
naturally industrial plumbism is now seen almost exclusively in males
of working age and occasionally in more elderly men some years after
exposure.   Under Sections 58 and 59 of the Factories Act, 1937, women
and young persons are prohibited from employment in the more dangerous
lead trades and in the others are subject to numerous restrictions.
This and similar previous legislation has resulted in industrial plumbism
in women being now practically non-existent, but Oliver (1939) related
to the author the prevalence of lead poisoning - especially
encephalopathy - among women in the last century and had frequently
observed their pronounced susceptibility to poisoning, even after a
short industrial exposure to lead.   In outbreaks of non-industrial
plumbism children have also been noted to have an increased susceptibility
(Aub et al., 1926).

Diagnosis.

Diagnosis of plumbism may be easy or exceptionally difficult.

There are many cases which do not conform to the typical description given in medical textbooks. Indeed, lead poisoning has been likened to syphilis (Lanza, 1935) in that it has a variety of effects on the human systems and can be dormant and unsuspected in the tissues for many years before showing itself. Again, like syphilis it may be a contributing cause of many a death for which it does not get its rightful share of the blame.

'Classical' Signs and Symptoms.

Among the classical findings in lead poisoning may be mentioned:

(1) Pallor of the skin.

(2) 'Lead line' on the gums.

(3) Constipation, anorexia and abdominal colic.

(4) Paralysis.

(5) Headache, general weakness, neuritis and joint pains.

(6) 'Encephalopathy'.

(7) Arteriosclerosis.

It should immediately be stressed that these seven headings are only certain manifestations of the disease; not one of them can be regarded in itself as proof of lead poisoning. A lead worker suffering from Addisonian anaemia would present a clinical picture including the majority of the above symptoms and signs. Too often is a man regarded as a case of lead poisoning merely on account of his occupation. A careful correlation of all clinical findings, together with results of laboratory tests is required. A diagnosis made

purely on laboratory findings is, however to be deprecated, as will be discussed later.

Certain of the clinical findings which can be associated with plumbism are subsequently considered in greater detail.

(1)   Pallor of the skin.

This is a most constant finding in lead poisoning, although asymptomatic lead workers may show it without suffering from any marked degree of anaemia, it being possibly due to vasomotor spasm of the arterioles caused by lead (Aub et al., 1926).   If, however, there is an accompanying low colour index anaemia with a high stippled cell count, marked polychromasia and reticulocytosis, this is very strong evidence in favour of plumbism.   Some chronic cases suffering from ill health (primarily caused by lead) may have little anaemia and no stippling of the erythrocytes.

(2)   Lead line in the gums.

The presence of a lead line on (or more correctly 'in') the gums indicates lead absorption but not necessarily poisoning.   It is never present on the gums of edentulous individuals.

As stated previously, the blue discoloration lies in the gingiva about $\frac{1}{2}$ - 1 mm. from the gum margin.   It is most obvious at the base of carious teeth, and such teeth may also show some degree of bluish discoloration.   Lead workers frequently have decayed teeth, the toxic action of lead, according to Aub, accounting for this.   A bluish discoloration of the buccal mucosa opposite carious teeth (Oliver's sign) has the same significance as the lead line on the gums.

Although not diagnostic of lead poisoning it is the author's opinion that if a lead line be found the individual is either suffering from plumbism or, if the same exposure to lead is continued, his health will be adversely affected. In many cases the lead line may be difficult to detect and is best demonstrated by inserting a piece of white paper between the gum and the teeth. Some authorities (Lane, 1939) state that it is impossible to discredit the presence of a lead line without in the first place having the teeth 'scaled' by a dentist.

(3) Abdominal colic and constipation.

Although not of serious consequence in itself lead colic is the most painful and dreaded symptom of lead poisoning. It is also one of the commonest manifestations of the disease. Anorexia, constipation and a foul taste in the mouth (which some patients describe as 'metallic') precede the onset of colic. The pain is usually situated around the umbilicus or in the hypogastrium, but may vary both in site and intensity. The attack of spasm may last two to five minutes or longer, and may recur every ten minutes or even more frequently. During the attack the patient is pale, covered with cold sweat and writhes in agony, being unable to keep still. He usually presses on his abdomen with his hands. The temperature is usually normal or subnormal, but may be raised by a degree or so (Aub). This was seen by the author in two cases. The pulse is somewhat slow. There is some degree of guarding of the abdominal muscles during an attack, with subsequent slight resistance of the abdominal wall, but this - and likewise tenderness - are never pronounced.

Differential diagnosis between lead colic and an acute abdominal surgical emergency is a matter of extreme importance. Renal colic has also to be excluded. The history, absence of marked tenderness, fever and rapid pulse, and examination of the urine and blood usually make the diagnosis clear. As a rule, stippled red cells are seen in lead colic, and there is no leucocytosis.

It is equally important, however, to remember that a lead worker is just as liable to acute appendicitis or perforated peptic ulcer as any one of the general population.

The pain is due to severe muscular contractions of the gut, and Aub (1926) is of the opinion that the most likely explanation of it is that lead acts directly on the smooth muscle of the intestine, producing increased tone and loss of motility. As a result of this, constipation occurs and the griping pain is due to reflex constriction which approaches this amotile hypertonic area. It is comparable to the pain of intestinal obstruction. There is some evidence, however, of the pain being due to action of lead on the vagus centre in the medulla or its action on the coeliac ganglion. The exact cause is unknown.

(4)   Lead Palsy.

This, the most incapacitating manifestation of lead intoxication, is now rarely seen; none of the cases described in this thesis showed palsy of the arms or legs, although several complained of 'weakness of limbs', which Legge (1934) regarded as a most important symptom. Opinions differ as to whether the primary lesion lies in the

muscle or nerve. Chronaximetric estimations carried out by Lane and Lewy (1935) suggest that at times the nervous elements are affected even in apparently healthy lead workers. In addition, the muscles are probably directly affected by lead to some extent.

According to Hunter (1936) lead palsy may develop during the first month of work or after many years of exposure. The commonest form is 'wrist drop' due to paralysis of the radial nerve. This type of paralysis usually begins in the long extensors of the fingers and then to the long extensors of the wrists. The supinator longus and the long abductor of the thumbs usually escape. 'Shoulder' palsy may occur at times as may atrophy of the thenar, hypothenar muscles and interossei. Lead palsy rarely affects the lower limbs but may do so - peroneal paralysis resulting in foot drop, a condition popularly known in Australia as "the dangles" (Nye, 1933). There is close correlation between the muscles most used and those affected by paralysis. Painters were more prone to wrist drop than file cutters, who developed palsy of the intrinsic muscles of the hand. (Hunter). The occurrence of ocular palsy due to lead has been stressed by Gibson (1931). Although there may be other manifestations of the disease such paralyses, especially in children, may be the only clinical signs.

(5) Arteriosclerosis.

Arteriosclerosis and its allied symptoms are stated to be frequently met with in chronic lead poisoning (Legge, 1934) but are not constant findings. One of the cases recorded by the author had chronic nephritis, hyperpiesis and died from cardiac defeat. In the

remaining cases hypertension and arteriosclerosis were absent.
These cases were, however, 'less chronic'.   Jones (1935) although
admitting that lead may be a factor in the above disturbances
considers that the importance of arteriosclerosis in plumbism is
stressed too much.   Undoubtedly cases do occur, and deaths due to
cerebral haemorrhage and coronary thrombosis in lead workers and
others may to some extent be primarily caused by the action of lead on
the kidneys or cardiovascular system.   As the above cardiovascular
catastrophes are common causes of death it is extremely difficult to
assess the importance of lead in these cases.   Teleky (1937) working
in Germany also found no appreciable evidence of increased blood
pressure and arteriosclerosis in lead workers as compared with members
of the general population of similar age groups.

(6)   Lead encephalopathy.

This was excellently described by Grisolle (1836) and since then
little has been added to the clinical description of this form of
lead intoxication.   Delirium, convulsions, coma, hallucinations,
diplopia, blindness, neuro-retinitis and papilloedema may occur, and
there may be paralysis of other cranial nerves and in the limbs.
The cerebro-spinal fluid is often under increased pressure and there
may be lymphocytic pleiocytosis.

Nowadays cases of lead encephalopathy are rare and most
of those recorded seem to be in children and of non-industrial origin.
In a case of this type recorded in this thesis the clinical picture
first suggested intracranial neoplasm, and the similarity between

these two conditions has been mentioned by Bramwell (1931), Porritt
(1931) and others.

(7)   Other clinical manifestations.

Headache, 'pains in the bones', cramps in the limbs,
irritability and palpitation may be quoted as examples of the many
less typical symptoms of increased lead absorption.   Bramwell and
Porritt record cases of plumbism in which the first diagnosis had
been nephritis, 'gastric disease', subacute combined degeneration of
the cord and 'idiopathic neuritis'.   Most of these cases were of
non-industrial origin, and they stress the importance of considering
plumbism as a diagnosis in cases of obscure illness.

Laboratory aids in diagnosis.

These are of value both as positive and negative evidence,
but as Kehoe (1933c) says, "the diagnosis of lead intoxication must
continue to rest upon skill and judgement in the elicitation and
interpretation of clinical evidence".   There has lately been an
increasing tendency to diagnose lead poisoning by laboratory tests.
Although such investigations may be of great value in assessing the
degree of lead exposure, too much importance should not be attached
to them when making a diagnosis.   They should always be taken into
consideration together with the history and clinical manifestations
of disease.

Haematological findings such as stippling of the erythrocytes,
polychromasia, a raised reticulocyte count or a markedly positive

basophilic aggregation test (McCord, Holden and Johnson, 1935)
may furnish valuable information, as may a raised blood lead value
or high amounts of lead in urine and faeces.   As already stated,
no definite limits can be placed, but the presence of more than 5,000
stippled cells (especially those with large granules) per million
erythrocytes, a blood lead value over $100 \mu g$. per 100 ml., a urinary
lead excretion of over 0.1 mg. per litre or a total lead excretion
of over 1 mg. per day, are all definite evidence of increased lead
absorption.   More than this one cannot say.

In Table VIII are recorded results of certain laboratory
tests carried out on thirty one patients, most of them hospital patients,
all with known or possible industrial contact with lead.   Although
lead poisoning was not a probably diagnosis in the majority of the
cases, the tests were of value in helping to exclude this possibility.
In none of the cases was the final diagnosis plumbism, although in
some instances it seemed possible that lead might have been a contribut-
ary factor to their illness.   The blood lead values varied between
40 and $187 \mu g$. per 100 ml. and 8 of them (25 per cent) had over $100 \mu g$.
Pb per 100 ml. of blood - the 'critical limit' of some other observers.
Two of them had a very small number of stippled cells in blood films
stained by alkaline methylene blue.

A consideration of these findings together with the results
recorded in Table VII show that marked variations in blood lead value
can be met with in those exposed to lead, and yet, in the author's
opinion, not be suffering from lead poisoning.   The same variations
occur with regard to analyses of excreta.

Table VIII.

Cases with known or possible increased lead exposure
examined and tested to exclude the possibility of
lead poisoning.

Case No.	Sex	Age	Occupation	Remarks	Blood lead μg. per 100 ml.
1.	M	26	Painter	Investigated for Mr. Scoular Buchanan. ? appendicitis or lead colic. No blue line on gums. Tender in lower abdomen, especially right iliac fossa. Temperature and pulse normal. Blood film: normochromic. No stippled cells seen. Appendicitis found at operation.	70
2.	M	17	Apprentice plumber	Headache for 2 years - sent by Dr. J. B. Gaylor for exclusion of lead poisoning. Does soldering with lead. No blue line on gums. General examination negative. Hb. 85%; R.B.C.s 4,850,000. Normochromic. No stippled cells seen.	74
3.	M	31	Lead works labourer	Exposed to risk of lead fume at work. In hospital on account of duodenal ulcer (confirmed by X-ray). Hb. 84%; Film normochromic. No stippled cells seen.	46
4.	F	24	Laboratory worker	Drop foot with numbness and tingling, 2 months duration. Diagnosis: disseminated sclerosis. Patient worked in laboratory of paint works - occasionally testing lead paint. Hb. 85%; Film normochromic. No stippling seen.	40
5.	M	17	Red leader	Working as red leader for 3 years. Developed weakness of legs, diplopia and scanning speech. Clinical diagnosis: disseminated sclerosis. Hb. 88%; R.B.C.s 4,860,000. W.B.C.s 6,200. No stippled cells seen. Retics > 1%. W.R. Negative.	68

Case No.	Sex	Age	Occupation	Remarks	Blood lead μg. per 100 ml.
6.	M	64	Master plumber	Investigated for Dr. Angus McNiven. Admitted to mental hospital in a confused state. Test performed to exclude lead encephalopathy. Blood film: normochromic. No stippled cells seen.	45
7.	M	66	Retired plumber	Retired for 4 years. Had painter's colic 30 years previously. Was mixing paints at that time. For 3 months before admission - rheumatic pains, headaches and weakness. False teeth. B.P. 185/110. Urine normal. Hb. 90%. Normochromic. No stippled cells seen.	75
8.	M	52	Bath enameller	Headaches and dizziness. Given up work on account of lead poisoning (??) a year previously. No blue line or other signs of plumbism. B.P. 140/90. Urine normal. Hb. 68%. No stippling seen. Hypochromic red cells.	49
9.	M	32	Red leader	Seen at Greenock Infirmary for Dr. J. Gracie. Difficulty in walking, and headaches. Diagnosis probably disseminated sclerosis. Used to work painting ship's hulls. No lead line on gums or other clinical signs of plumbism. Hb. 84%. No stippling seen. Retics $>$ 1%	40
10.	M	36	Soldier	Used to work in lead factory where "there was much dust". Present complaint tinnitus of 3 weeks' duration. No lead line on gums or other evidence of plumbism. Hb. 92%. No stippled cells seen. Retics 1.25 %.	130

Case No.	Sex	Age	Occupation	Remarks	Blood lead μg. per 100 ml.
11.	M	35	Red leader	"Gluteal fibrositis". General condition good. Hb. 86%. Normochromic. No stippling seen.	102
12.	M	58	Painter	Peptic ulcer (confirmed by X-ray). Hb. 81%. Normochromic. No stippling.	115
13.	M	36	Dock labourer	In hospital on account of duodenal ulcer, confirmed by X-ray. Exposed to lead dust at his work. Also did painting previously. Hb. 84%. No stippling. Normochromic.	132
14.	M	43	Red leader	Painting ships since 1918. Careful as regards toilet. No "dry rubbing down". Hb. 90%. Normochromic. No stippling seen.	75
15.	M	54	Red leader	Sent for examination by Prof. Ballantyne. Painting ships for 30 years. Attending hospital on account of dystrophy of eye. W.R. Negative. Hb. 93%; R.B.C.s 4,430,000. W.B.C.s 7,400. Normochromic. No stippling. Reticulocytes $>$1%.	64
16.	M	37	Electric welder	Asymptomatic. Sometimes exposed to fume coming from lead paint when at work. Had indigestion. Hb. 88%; R.B.C.s 4,610,000. W.B.C.s 8,200. No stippling seen. Reticulocytes $>$1%	79
17.	M	46	Plater	In hospital on account of bronchitis. Had used oxy-acetylene lamp on plates painted with red lead. Hb. 84%. No stippling seen. Reticulocytes $>$1%.	.124

Case No.	Sex	Age	Occupation	Remarks	Blood lead μg. per 100 ml.
18.	M	59	Plumber	Diagnosis: Paget's disease of bone. Had done a good deal of lead pipe soldering and lead burning. Hb. 75%; R.B.C.s 4,860,000. Normochromic. No stippling. Reticulocytes 1%.	109
19.	M	18	Apprentice plumber	Acute nephritis. Never done work with lead to any great extent. Hb. 86%. Normochromic. No stippling seen. Reticulocytes 1.5%.	43
20.	M	57	Painter	Painter for 30 years. Mixed and did dry rubbing down. Symptoms of peptic ulcer. Hb. 89%. No stippling. Reticulocytes > 1%.	187
21.	M	18	Apprentice plumber	Subacute appendicitis. Nothing suggestive of plumbism in general examination. Hb. 98%. Normochromic. No stippling. Reticulocytes > 1%.	83
22.	M	61	Scrap metal merchant	Infective arthritis. Nothing suggestive of plumbism clinically. Hb. 79%. R.B.C.s 4,650,000. W.B.C.s 8,200. No stippled cells seen. Reticulocytes 1%.	69
23.	M	42	Unemployed (ex sailor)	A case of progressive muscular atrophy. Had been regarded as plumbism previously, as he had done painting. Hb. 92%. Films: normochromic. No stippling. Reticulocytes > 1%.	58
24.	M	59	Unemployed (ex-lead sprayer)	Admitted on account of alcohol poisoning. Stated that 2 years ago he had suffered from plumbism. Nothing clinically to suggest this. Hb. 86%. No stippling.	47

Case No.	Sex	Age	Occupation	Remarks	Blood lead μg. per 100 ml.
25.	M	49	Painter	Does not mix paints. Sometimes gets hands and clothing covered with paint. Admitted to hospital suffering from urticaria.	85
26.	M	41	Riveter	'Indigestion'. Works on ship where welding and riveting is done through lead paint, with fume. Hb. 89%. Normochromic. No stippling.	41
27.	M	58	Painter	Arteriosclerosis and high blood pressure. Saphenous thrombosis. Hb. 85%. Normochromic. No stippling seen. Retics 1.5%.	71
28.	M	54	Painter	Headaches for two years. B.P. 146/90. Normochromic film. No stippling seen.	57
29.	M	42	Red leader	'Lumbago'. Hb. 96%. Normochromic film. No stippling. Retics 1%.	92
30.	M	50	Red leader	General weakness and dizziness. B.P. 165/95. No blue line or paralysis. Normochromic. Very scanty stippled cells.	122
31.	M	18	Painter	Abdominal tuberculosis (proved at laparotomy). Hb. 98%. No stippling. Retics 1%.	75

German workers (e.g. Taeger and Schmitt, 1937) have stressed the value of the presence of porphyrinuria in the diagnosis of plumbism. The author has no experience of this test, and a recent article (Chandler, Harrison and Rimington, 1939) shows that its value is probably slight.

In children, X-rays may be of diagnostic value (Vogt, 1930. Rodgers, Peck and Jupe, 1934). A lead line may at times be found near the epiphysis.

It is thus seen that, although one can test for evidence of increased lead absorption a definite diagnosis of plumbism cannot be made on these investigations alone. Such investigations, and probability, may be of great value in forming an opinion with regard to a case, but the final diagnosis should always be clinical.

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THE TREATMENT OF LEAD POISONING.

This can be considered under two headings - (1) Preventive
and (2) Symptomatic.

Preventive Measures.

Legislation has been the main factor concerned with the
fall in incidence of plumbism since the beginning of the twentieth
century.   Under Section 79 of the Factory and Workshop Act, 1901,
industrial lead poisoning became a notifiable disease under the
attention of the Home Office.   It is now notifiable under Section
3 of the Lead Paint (Protection against Poisoning) Act, 1926, and
Section 66 of the Factories Act, 1937.   Such notification should be
sent to the Chief Inspector of Factories, Home Office, Whitehall,
London, S.W.1. and not to the local Medical Officer of Health as
sometimes occurs.   Other Acts of Parliament and Home Office publications
and pamphlets have also helped to a great extent in lessening the
incidence of the disease.   As examples of these may be quoted the
"Memorandum on the dangers of lead poisoning in shipbreaking yards"
(1925), the Lead Paint Regulations 1927, " Painter's colic; how
caused and how best prevented" 1927, and "A guide to the Factories
Act, 1937".

The Factories Act makes special provisions concerning
working conditions in factories where lead is used, and the employment
of women and young persons in dangerous lead trades.   Such persons
are excluded from many occupations involving exposure to lead and

can only be employed in certain other processes.   The provisions
of the 1937 Act are more stringent than the previous legal measures.

With regard to non-industrial plumbism, legislation such
as the Pharmacy and Poisons Act, 1933 and the Poisons Rules, 1935
prevent lead preparations being obtained without a necessary
prescription, and the Public Health (Preservatives etc. in Food)
Regulations, 1925, forbid the use of lead compounds as colouring
mattersfor foods.   The Food and Drugs Act, 1938 forbids the sale
of food "injurious to health" and so excludes lead in quantity.
Although, as previously mentioned, there is no legal limit for
lead in drinking water, local authorities in their regular analyses
of supplies usually keep a guard against this possible contamination.

Again considering industrial plumbism, modification of
processes - such as the manufacture of leadless or silica fritted
glazes in the pottery industry - have also caused a reduction in the
incidence of plumbism.   Improved factory conditions with special
regard to ventilation and avoidance of dust have played a most
important part in prevention of the disease.   The employment of respirators,
'wet methods' and local exhaust ventilation are of prime importance.
Lane (1936a) advocates the employment of 'exhausted blow pipes'
by lead burners.   This overcomes the production of fume encountered
in this very dangerous process.   He showed his methods to the author
and demonstrated the other excellent preventive measures employed
by the Chloride Electrical Storage Company at Clifton, near Manchester.
In certain other factories visited, however, the standards were not
so high.

Regular medical examination of lead workers enables examining surgeons under the Factories Act to detect men showing evidence of increased lead absorption. In addition to routine observations, the regular examination of blood films for increased numbers of stippled red cells (Lane, 1936b) or the analysis of blood and/or excreta for lead content are of definite value.

The employment of clean, sensible men in lead trades is also important, as is the fact that they should be temperate. Anyone showing a family tendency to the disease should, according to Lane, be considered unsuitable for lead work. Working time should not exceed eight hours per day. Adequate provision of cloakrooms, canteens, washrooms and changes of clothing also play their part in the prevention of the disease. A regular daily intake of one pint of milk, as already discussed, is also of value.

The Home Office Industrial Museum in Horseferry Road, London S.W.1., which was opened in 1927, affords employers, employees and others opportunities of seeing and obtaining information regarding methods, arrangements and appliances for promoting safety, health and welfare of industrial workers.

In the prevention of industrial plumbism and other industrial diseases the maxim of the late Sir Thomas Legge might well be borne in mind - "If you can bring an influence to bear external to the workman (i.e. one over which he has no control) you will be successful, but if you cannot, or do not, you will never be wholly successful".

Symptomatic treatment.

Various methods of treatment of lead colic employing
drastic purgatives (e.g. croton oil), carminatives, alum and
"macaroni" (a mixture of antimony and sugar) were employed by
physicians in the 18th and 19th centuries, sulphuric acid, lemonade
and potassium iodide becoming recognised in the 19th century as
having properties to cause elimination of lead from the body.
Encephalopathy and palsy were also treated with numerous drugs,
without much success (Grisolle, 1836).   Oliver (1914) advocated
bi-polar baths by the use of which he claimed that lead could be
removed from the body by electrolysis, but these have since been
shown to be of no value.

Modern research has resulted in improvements in treatment
of the acute manifestations of plumbism and also in the prognosis of
the disease.   Sir Thomas Legge (1934) made the unqualified statement
that lead poisoning was never cured.   This was the opinion of a man who
was mainly an administrator and who had a wide experience of
epidemiology of plumbism.   His view is undoubtedly correct with regard
to many of the severe cases met with in the past, but, as is shown in
several cases described by the author, apparently complete recoveries
can occur although it is admitted that such individuals will have an
excessive amount of lead in the body for the rest of their lives.
Whether or not this lead does harm depends on its distribution between
soft tissues and the skeleton.   Lead laid down in the bones produces
no ill-effects - only that in the circulation and the soft tissues

can cause cellular damage and ill-health (Aub, 1926, 1935).

Following on the observations already discussed, that
calcium and lead metabolism were closely allied, treatment of lead
poisoning by a high calcium intake was advocated. This has given
very successful results both in the prevention and symptomatic
treatment of plumbism (Aub, 1926, 1935. Belknap, 1935. Hunter,
1936).

Under such conditions lead is deposited in the bones where,
if a positive calcium balance is maintained, it remains innocuous.
Under conditions of metabolic upset, however, (e.g. if the diet be
lacking in calcium or if for some reason the pH of the blood is
altered) the stored lead is mobilised and returns into the blood stream
where it may give rise to further symptoms.

Some authorities (Aub, 1935) regard large amounts of lead
in the bones as a potential danger, and advocate 'de-leading' measures
involving the use of drugs in conjunction with, or without, a low
calcium diet in order to increase lead excretion. This should always
be done in hospital and under careful laboratory control, as on
occasion a return of symptoms of plumbism has been associated with
this sudden mobilisation of lead. Should this occur 'de-leading'
should be stopped and an immediate return to a high calcium diet
ordered.

Although there is agreement that a high calcium intake is
indicated during the toxic episodes of plumbism, there are, however,
two schools of thought regarding subsequent treatment. Some writers

maintain that a high calcium diet should be continued, believing
that de-leading may do harm whilst others, although admitting that
return of symptoms may occur during treatment, consider the risk
negligible as compared with the ultimate clinical improvement resulting
from increased excretion of lead.   The author agrees with Aub in
this latter view, although each case has to be taken on its own merits.
Where there has been a relatively prolonged exposure to lead, causing
symptoms in a young or middle aged man, de-leading should be
considered.   In older patients it is as a rule an unwarranted
procedure.   The same applies to children (Aub, 1935) who should
never be placed on a low calcium intake, and also to individuals
in whom there are signs of renal insufficiency.

Table IX shows a typical high calcium diet as used by the
author in the treatment of lead poisoning.   It contains 2.692 g. calcium
per day.   In many cases parenteral calcium in the form of calcium
gluconate, 10 ml. 5 per cent solution intramuscularly, was also given
once or twice a day.   During colic 10 - 20 ml. of this solution was
injected slowly into a vein.   In several cases the result was
remarkable - the pain being immediately relieved, sometimes before
the injection was completed.   Several injections may be required.

The relief of lead colic by calcium therapy involves more
than the mere tendency of calcium to favour storage of lead.   There
is evidently an anti-spasmodic action on involuntary muscle as well.
The author has also seen this same action employing intravenous calcium
treatment in cases of renal colic and epididymitis.   Calcium lactate,

Table IX.
HIGH CALCIUM DIET

Food	Breakfast	Dinner	Tea	Supper	Total gms.	Calcium gms.
Vegetables 3%		Cabbage 100		Salad { Lettuce, Nuts, Raisins, Dates }	100	.045 .012 .006 .015
Vegetables 6%		200			200	.028
Potatoes		200			200	
Fruit 10%	Orange 200			Orange 200	400	.180
Fruit 7.5%		Grapefruit 100			100	.021
Wholemeal bread	60		60	60	180	.141
Skim milk	500	300	300	400	1500	1.581
Eggs	1			1	2	.080
Meat		90			90	.014
Cheese			60		60	.558
Butter	20		20	20	60	.009
				Sugar 100 Jelly 30	100 30	.009

Ordinary cooking salt used.

Total gms. Calcium 2.692

in doses of up to 60 grains t.i.d. has been advocated in the treatment of plumbism.   In some of the cases recorded in this work this has been employed, but usually in smaller doses in conjunction with two pints of milk a day.   Milk is probably the best form of prescribing oral calcium.

Severe cases often require the hypodermic injection of atropine, gr. 1/60 and morphia gr. $\frac{1}{4}$, which may have to be repeated. Hot cloths to the abdomen, oral magnesium sulphate and carminatives, and olive oil enemata are also important in treatment of the toxic episodes.   An iron mixture should be prescribed after the bowels have become more regular.

After two or three weeks on high calcium intake, and when all acute symptoms have subsided, 'de-leading',if considered advisable should be instituted in order to increase lead excretion.   Although not absolutely necessary (Tompsett, 1939c) this treatment is best carried out when the patient is on a low calcium diet.   Such a diet (Table X) by itself can cause increase in the excretion of lead, but the effect is enhanced by the oral administration of drugs such as potassium iodide gr. xx q.i.d., ammonium chloride gr. xv or more q.i.d., or dilute acids (acid phosph. dil., acid hydrochlor. dil. or acid sulph. dil.) in drachm doses q.i.d. (Aub, 1926, 1935).   Sodium bicarbonate gr. 60 or more q.i.d. has a similar effect (Litzner, Weyrauch and Barth, 1931, Tompsett 1939c).

Intramuscular injections of parathyroid extract (parathormone) in doses of about 50 units per day, which is best given in two doses,

Table X.
LOW CALCIUM DIET

Food.	Breakfast	Dinner	Tea	Supper	Total gms.	Calcium gms.
Vegetables 5%			Tomato 100		100	.011
Rice or macaroni						-
Fruit 15%		Stewed apple 200 Sugar 15			215	.014
Fruit 20%				Banana 100	100	.009
White bread	50		50	50	150	.033
Cream 40%	30		30	60	60	.040
Meat		60			60	.008
Bacon	100				100	.006
Cold ham				60	60	.006
Salt-free butter	10		10	10	50	.005
				Sugar	100	-
				Syrup	30	.001

Salt used pure NaCl

Total gms. Calcium   0.151

have also the effect of increasing lead excretion when the patient
is on a low calcium diet.   Calcium - and likewise lead - is drawn
from the bones and excreted in the urine (Hunter and Aub, 1927).
As a rule, however, only the first course of parathormone has this
effect whereas, as shown in this thesis, acidosis-producing substances
can effect mobilisation of lead several times in the same case.   They
are moreover much cheaper and more reliable than parathormone.   Oral
parathyroid extracts are valueless.

Such de-leading should only be done in hospital where the
case can be carefully observed.   When parathormone is used frequent
serum calcium estimations should be performed, and this value should
not rise over 14 mg. per 100 ml.   Any return of toxic symptoms calls
for an immediate return to high calcium intake.   If acidosis-producing
substances, potassium iodide or sodium bicarbonate are employed the
same care is needed, and when using the former drugs any symptoms
indicating severe depletion of the alkali reserve call for cessation
of such treatment and the giving of alkalies and glucose.

As a rule one or two courses of de-leading, each lasting
one to two weeks cause marked improvement, although the duration of
treatment and results naturally vary in individual cases.   Thereafter
a return to high calcium intake should be made and the patient
maintained on a diet containing at least a pint of milk a day.   Extra
milk should be given in any other illness which he may suffer from
subsequently.

Many cases remain asymptomatic after such treatment, although,

perhaps years later, an alcoholic bout, an inadequate diet and an
acute illness may cause symptoms to return.   High calcium intake
is again indicated in these cases.

During the development of lead palsy a high calcium diet
should be used to favour storage of lead.   In the early stages 'cock
up' splints (e.g. for wrist drop) are needed and massage and strychnine
are also recommended.   Mild electrical stimulation of muscles by
an induction coil is said to be of value.   In many cases full power
of the muscles never returns, although marked improvement often
occurs.

Treatment in cases of lead encephalopathy is of little
value.   High calcium diet was of no value in the case recorded by the
author in this thesis, even though it had the effect of lowering the
blood lead value.   Hunter (1936) mentions that this treatment has
on occasion been effective in America.

Finally, in all cases who have suffered from the effects of
increased lead absorption should have regular blood counts and, if
possible, analyses of the blood for lead.   Lead anaemia is very stubborn
to treatment.   Prolonged courses of iron are needed, and at times
combined 'iron and liver' therapy, although unscientific, gives
satisfactory results.

The symptomatic treatment of plumbism can be summarised as
follows:

For the toxic episodes: HIGH CALCIUM INTAKE (oral and parenteral)
                          Saline purgatives
                          Olive oil enemata
                          Sedatives

Paralysis or other local manifestations
should receive appropriate treatment in
conjunction with the foregoing.

Subsequently: the patient should be maintained on a diet containing

at least one pint of milk a day, together with other substances

(e.g. cheese and oatmeal) which are rich in calcium.

If considered advisable (there being no evidence of renal

insufficiency) 'de-leading', employing a low calcium diet and

ammonium chloride gr. xv q.i.d. should be instituted after all acute

symptoms have subsided.   This treatment lasts 6-14 days and may be

repeated.   It should be stopped if symptoms recur.

A return should then be made to a high calcium intake,

which should be maintained.

CASES OF INCREASED LEAD ABSORPTION

AND LEAD POISONING.

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CASES OF INDUSTRIAL ORIGIN.

"........... namque cum fudendo plumbum
flatur, vapor ex eo insidiens corporis
artus et in diet exurens eripit ex
membris eorum sanguinis virtutes."

Vitruvius (c.35 B.C.)

Translated by Morgan (1914):

"........... for when lead is smelted in
casting, the fumes from it settle upon
their members and day after day burn
out and take away all the virtues of the
blood from their limbs."

Case 1.

Industrial lead poisoning due to paint.

An Irishman, aged 32, whose occupation was that of a 'red-leader' (i.e. painting ships with red lead paint) was admitted to the Western Infirmary, Glasgow, under Dr. G. A. Allan complaining of abdominal colic and general weakness.   He was investigated and treated by the author.

Case History:

For nine weeks he had been painting ships in a Clyde shipyard. He stated that he worked in confined, ill-ventilated "tanks" in ships under construction, and that "paint was everywhere"; he frequently mixed paints and worked on surfaces above his head, getting covered with paint in the process.   He himself admitted that he never took any great precautions to avoid the danger of paint on his person and he hardly ever washed his hands before taking food.   He smoked at work.   His appearance on admission (on account of symptoms he came straight from work) was in keeping with the history, his clothing, face and hands being filthy with red lead paint.

For a month before admission he had not felt well, and on account of constipation had been taking 'medicine' to correct this. He had also felt weak, having lost colour, and suffered from headaches.   For three weeks he had complained of an occasional numb feeling in his right hand, especially the ring and little fingers, and stated that "he hadn't the same control over his brush when working".

During the ten days immediately before admission he had suffered from spasms of pain low in the abdomen, lasting two or three minutes. These had become more severe and more frequent.

Previous health and personal history:

Apart from gonorrhoea eleven years previously he had always been healthy. He had worked in a paint works for a short time when aged 22, where he had mixed paints and had never suffered from ill-effects. Subsequently he had worked as a plater's helper, where there was, according to the patient, no lead risk. He had always been "easy-going" and smoked and drank a good deal. He wasn't particular about personal hygiene.

Clinical examination:

On admission, temperature and pulse were normal. He looked pale and ill, and was obviously in pain. He was of thin build. The conjunctivae were pale, there was slight guarding of the abdomen, but this was not pronounced. He indicated the site of pain as just below the umbilicus and, when a spasm came on, held his abdomen with the hands, which afforded some relief.

His tongue was moist and covered with a brownish fur posteriorly. His breath was offensive. Several teeth were carious and there was a definite 'lead line' on the gum margins in both jaws.

There was no evidence of arteriosclerosis and his blood pressure was 115/70. His heart sounds were regular and of moderate tone. No abnormality of the lungs was detected.

Although he complained of numbness in his right hand, no

evidence of organic nervous change could be found.   Sensation and
reflexes were normal, and the extensor power of both wrists was
equal and satisfactory.

Special investigations:

Blood count: Red blood cells 3,810,000
                Haemoglobin 65 per cent
                Colour index 0.85
                White blood cells 9,400
                Polymorphs. 60.5
                Lymphocytes 28.5
                Monocytes   10.0
                Eosinophils   1.0
                Basophils   nil

Films stained by Leishman's method showed stippling of the
erythrocytes (5,600 per million red cells: large, medium and small)
and also frequent polychromasia.   The red cells appeared of average
size, although there was slight poikilocytosis.   A differential
leucocyte count showed no abnormality.   A reticulocyte count was
not performed.

Blood lead value: 380μg. per 100 ml.

Blood urea: 28 mg. per 100 ml.

Wassermann reaction: Negative.

The urine was normal by routine side-room tests.

Treatment and progress:

The patient was given enemata and salines, with a high
calcium diet and daily intramuscular injections of 10 ml. 5 per cent
calcium gluconate.   He rapidly showed considerable clinical
improvement.   Abdominal symptoms were absent within 24 hours of
commencing treatment.   Parenteral calcium was stopped after six

days, but high calcium diet was maintained for a fortnight. The
blood lead value had fallen to 267 μg. per 100 ml. by this time.

At this stage a low calcium intake together with ammonium
chloride, 1 g. q.i.d. was prescribed in order to increase lead
excretion. Excreta had been collected over a three-day period at
the end of the time of high calcium intake, and this procedure was
continued during the de-leading treatment. Faeces and urine were separ-
ately 'pooled' in three-day amounts, and the average daily lead
content of each was estimated.

Results of analysis of the excreta together with blood lead
values and treatment at various stages are recorded in Table XI and
graphically represented in Charts 4. and 5.

The treatment was associated with no apparent clinical
ill effects and was well tolerated. The patient stated that he felt
much better. There had been no albuminuria. The blood urea was
36 mg. per 100 ml. Stippled erythrocytes had shown no increase since
admission. The blood count by that time was:

                R.B.C.s   4,230,000
                Hb.   74 per cent
                C.I.   0.87
                W.B.C.s   8,100

Occasional stippled erythrocytes and polychromatic cells were seen
in Leishman stained blood films, but were too infrequent to estimate.

The patient was dismissed from hospital five weeks after
admission, feeling greatly benefited from the treatment. His general
condition was much better although he still looked pale and the lead
line on the gums was still present, though much fainter.

Table XI.

Three day period	Blood lead value μg. per 100 ml.	Average daily faecal excretion of Pb. (mg.)	Average daily urinary excretion of Pb. (mg.)	Average total daily excretion of Pb. (mg.)	Calcium intake.
1.	267	0.16	0.61	1.25 (over 6 days)	HIGH
2.	–	1.84	0.69		
3.	252	1.30	0.24		
4.	–	1.33	0.28	2.15 (over 9 days)	LOW + NH_4Cl
5.	267	3.00	0.24		
6.	165	1.32	0.06	0.92 (over 6 days)	HIGH
7.	–	0.28	0.18		
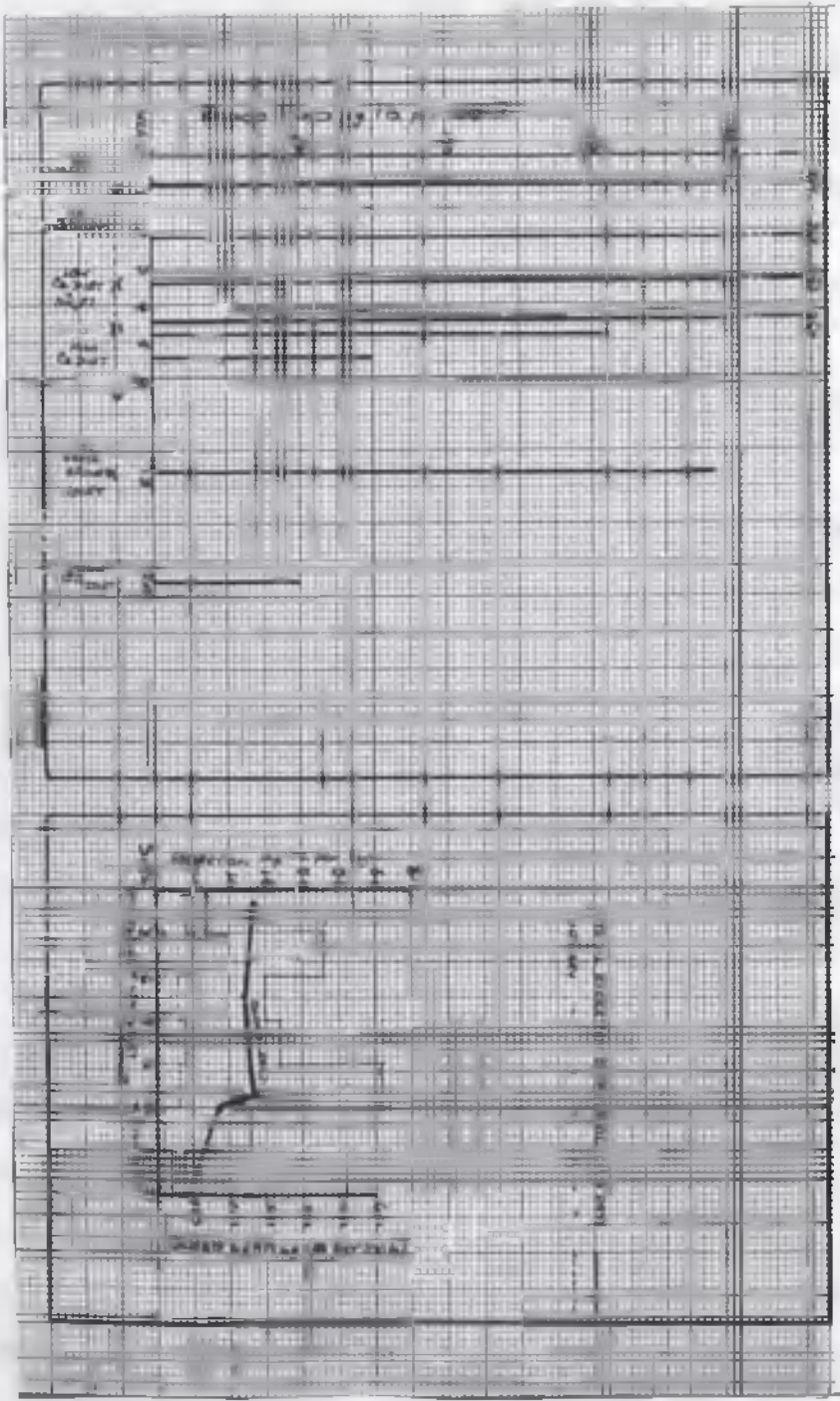
CHART 4.

CHART 5.

He was told to continue taking large amounts of milk and cheese every day. An iron mixture and magnesium sulphate were also prescribed.

He reported to hospital five weeks later, and stated that he had kept well. The lead line was still present, although much less obvious. Blood count figures at this time were:

```
R.B.C.s    4,490,000
Hb.        75 per cent
C.I.       0.84
W.B.C.s    5,300
```

No stippled cells could be found after a prolonged search (Leishman). The blood lead value had risen to 201 μg. per 100 ml. He admitted not having kept to the diet prescribed and had not even taken any medicine. He had also been drinking beer and spirits regularly, having been drunk on several occasions. He was cautioned as to the danger of this and re-advised regarding his habits.

Three months later the blood count had improved to:

```
R.B.C.s    4,520,000
Hb.        82 per cent
C.I.       0.91
W.B.C.s    5,600
```

Blood films stained by the Leishman and alkaline methylene blue methods failed to detect any stippled erythrocytes. The blood lead value was 49 μg. per 100 ml.

Clinically he had again improved, his colour being much better. No lead line was visible on his gums. He complained of cough and spit, however, but an X-ray of his chest showed no signs of organic disease in the lungs. He was anxious to re-start work but

was advised to give up painting and all other work where there might
be a lead hazard.   Considering the patient's general attitude to
life it was doubtful if this advice were taken as although he had
stated he would be temperate, his promises were not carried out.

Remarks on the case.

This man's illness was largely due to his own lack of care
and stupidity.   His appearance on admission was strongly suggestive
of a diagnosis of lead poisoning, and biochemical and haematological
results confirmed this.   Symptoms were quickly relieved by high
calcium intake and caused a fall in blood lead value.   De-leading,
carried out under careful observation, caused no ill-effects.
Although there was no apparent rise in blood lead value at the time
of the tests, total excretion of lead was increased by about 70 per
cent per day.   This man had a comparatively short exposure to lead
and may not have had appreciable quantities of lead in the bones
which could be mobilised;   this may have accounted for the blood lead
value failing to rise.

Great variation in the amount of lead excreted in faeces
and urine during several three-day periods was noted, independent of
treatment.   During the period of increased excretion the faeces were
found to contain most of the lead.   Actually, higher amounts were
found in the urine on high calcium intake than when 'de-leading'.

The results obtained do not stand up to a severe statistical
criticism but, on the whole, are significant.   Although after discharge
from hospital the blood lead value had risen there was no recurrence of

symptoms. Although proving rather resistant to iron therapy the anaemia gradually improved, and two months after discharge from hospital no stippled cells could be found in the blood. There was never any evidence of renal involvement in this case.

Case 2.

Lead poisoning due to employment in an accumulator works.

A married man, aged 29, complaining of general weakness and
attacks of abdominal pain, was seen by the author at an outpatient
clinic at the Western Infirmary, Glasgow.   He had been employed as
a lead burner in accumulator factories for the previous 7 years.
He was admitted to Dr. G. A. Allan's ward, where the author was given
facilities to investigate and test the case.

Case history:

The patient stated that he had been losing colour for about
three months, but had only felt ill for about four weeks.   During that
time he had suffered from general weakness, lassitude and headaches.
There had been a foul taste in his mouth and the bowels had been
constipated.   During the ten days before admission colicky pains had
developed, the attacks coming on every hour or two and lasting for
five or ten minutes.   On several occasions these attacks "had doubled
him up" with pain, but the majority had not been very severe.   There
had been no vomiting.   He had also complained of a numb feeling in
his arms and legs.

Previous health and personal history:

Apart from an abscess in the region of his left knee, for
which he had been operated on in 1912, he had always enjoyed good
health.   He had been a lead burner in various electric battery works
since 1930.   During the course of his work he had been exposed to lead

fume and had never worn a respirator.   The factories in which he had worked were small concerns and, although seen weekly by examining surgeons under the Factories Acts, the companies concerned did not seem to bother about the health of their employees to any extent.

He took alcohol regularly and while unwell had been taking even more than usual.   He had never taken extra quantities of milk in his diet.

Clinical examination:

The man was of large muscular build.   On admission he appeared pale, the face having an ashen-grey colour and the mucous membranes showing pallor.   His temperature and respiration rate were normal.   There was no cyanosis, oedema or jaundice.   The pulse was regular and rather slow, being 62 per minute.   He had no really severe attacks of colic when under observation, but complained of a gnawing pain coming on periodically in the hypogastrium and left flank.

He had numerous carious teeth and the gums of both jaws showed a well defined lead line.   The tongue was dry and covered with a grey fur.   The abdomen was lax and free from tenderness, there being appreciable splenic or hepatic enlargement.   Heart sounds were pure and of moderate tone..   Blood pressure was 125/75.   There was no clinical evidence of arteriosclerosis.   The lungs were clear. Examination of the nervous system was negative, reflexes and sensation tests being normal.   There appeared to be no extensor weakness of the wrists, and both grips were strong and equal.

Special investigations (on admission):

<div style="padding-left:2em">

Blood count: Red blood cells 3,010,000
Haemoglobin 58 per cent
Colour index 0.96
White blood cells 6,600
Polymorphs. 64.0
Lymphocytes. 26.0
Monocytes   9.5
Eosinophils   0.5
Basophils   nil

</div>

Films stained by Leishman's method showed that stippling of the erythrocytes was present (7,000 per million red cells: large and medium). Most of these cells contained large granules. Polychromatic cells were also frequently seen and, although most of the remaining red cells were normochromic, there was some degree of anisocytosis and poikilocytosis. A reticulocyte count was not performed.

Blood lead value: 346 μg. per 100 ml.

Blood urea: 38 mg. per 100 ml.

Wassermann reaction: Negative.

The urine was normal by the ordinary side-room tests.

Treatment and progress:

Salines and enemata were given and the patient put on a high calcium diet, together with daily intramuscular injections of 10 ml. 5 per cent calcium gluconate. With this treatment, although the patient complained of a feeling of "discomfort" in the abdomen no further attacks of severe pain occurred. The discomfort disappeared after three days of treatment and subsequently there was maintained clinical improvement; at the end of a week the blood lead value had fallen to 87 μg. per 100 ml. After a further week on a

high calcium diet (without parenteral injection) it had risen to
174 μg. per 100 ml.   Stippled red cells were present in the blood
in about the same numbers as when admitted.   At this stage a course
of de-leading treatment was instituted, the patient being placed on
a low calcium diet together with 1 g. ammonium chloride q.i.d. orally.

All excreta had been collected during the last three days
of high calcium therapy and this was continued during the period of
de-leading.   Urine and faeces were separately 'pooled' into three-
day samples and the lead content estimated.   The results of total
excretion of lead, as judged by analysis of 'three-day samples' are
recorded in Table XII, together with blood lead values in relation
to treatment.   They are shown in graphical form in Charts 6 and 7.

No ill-effects had been noticed during treatment, even when
the blood lead value was very high.   There was no increase of stippled
erythrocytes in the blood when this occurred, the count of these cells
actually having fallen to 1,500 per million erythrocytes (Leishman).
Urinary output had varied from 38 to 64 ounces per day, showing no
correlation to treatment.   There had been no albuminuria, and the blood
urea figure was 42 μg. per 100 ml.

After being on a high calcium intake for another week the
patient was discharged from hospital.   He felt very much improved
although he still looked pale.   Blood count figures were:

<pre>
        R.B.C.s   3,400,000
        Hb.   63 per cent
        C. I.   0.93
        W.B.C.s.   6,200
</pre>

Occasional stippled cells (with large or medium granules) were seen
(Leishman).

Table XII.

Three day period	Blood lead value g. per 100 ml.	Average daily faecal excretion of Pb. (mg.)	Average daily urinary excretion of Pb. (mg.)	Average total daily excretion of Pb. (mg.)	Calcium intake.
1.	87	0.47	0.30	0.81 (over 6 days)	HIGH
2.	174	0.88	0.16		
3.	-	1.61	0.34	1.57 (over 9 days)	LOW $+ NH_4Cl$
4.	1559	1.28	0.33		
5.	3650	0.98	0.18		
6.	56	0.75	0.07	0.63 (over 8 days)	HIGH
7.	-	0.12	0.31		

CHART 8.

CHART 7.

He was instructed to continue on a high milk intake, and iron and Epsom salts were also prescribed. The lead line was still evident on his gums.

Three weeks later he reported for re-examination. The lead line was still faintly present on his gums. He had no complaints and stated that he felt much stronger. He had not, however, been keeping very conscientiously to the diet prescribed. His colour was better and the blood count was:

```
R.B.C.s    3,520,000
Hb.        72 per cent
C.I.       1.0 (approx).
W.B.C.s    5,800
```

The blood lead value was 128 μg. per 100 ml. Very occasional stippled and polychromatic cells were present in Leishman stained blood films. The red cells were of more normal colour than previously.

A month later he reported again. Further improvement was apparent; there was no change in the blood count figures, however, an odd stippled cell being found in Leishman stained blood films. The blood lead value was 120 μg. per 100 ml. The lead line was very faintly seen on the gums. Larger doses of iron were prescribed.

At the end of another two months he was re-tested and the blood count was:

```
R.B.C.s    4,410,000
Hb.        91 per cent
C.I.       1.03
W.B.C.s    5,700
```

Reticulocytes   1 per cent

Blood films stained by Leishman's method and by alkaline methylene blue failed to show any stippled cells.   The blood lead value was 110 μg. per 100 ml.

His general condition was very satisfactory.   The lead line on his gums had disappeared.   He was advised to have his teeth extracted.   Although still rather pale looking his mucous membranes were well coloured.   Physical examination showed no abnormalities, blood pressure being 120/70 and his urine being normal.   He was advised never to return to work where he would be exposed to a 'lead risk'.

Remarks on the case:

This man had been exposed to lead in industry for seven years but had only shown symptoms for about a month.   Diagnosis was made clinically and confirmed by haematological and biochemical investigations.   His symptoms quickly disappeared after he was placed on a high calcium intake.

As a lead burner he had been exposed to the most dangerous form of lead - lead fume - and the relatively high amounts of lead present in his body were shown by the raised blood lead values and the raised lead excretion figures, especially during the period of de-leading.   Even though very high amounts were present in the blood during this treatment the patient never showed a return of symptoms.   Excretion of lead was increased on the average by nearly 100 per cent per day by low calcium intake and oral ammonium chloride.   Most of this increase occurred in faecal excretion.   There was considerable variation in

both urinary and faecal lead, when on either a high or low calcium diet, and the results have to be interpreted bearing this in mind.

Numbers of stippled erythrocytes declined as the blood count improved, and they had disappeared four months after exposure to lead had ceased.

Following treatment, general examination was entirely satisfactory. There was no evidence of organic changes in the cardio-vascular, renal or nervous systems. Although he still probably had increased amounts of lead in his body, especially in the bones, he showed no evidence of chronic poisoning and was asymptomatic.

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a day. He had always been temperate.

On admission to hospital the man said that he had been right for a month but that it was only for 3 days that he had really ill. In that time he had felt sick off and off and had been constipated. He had suffered from vague abdominal pains had become much worse on the day before admission, making him unable to work. The doctor had been called in, and he found

Case 3.

Industrial lead poisoning due to oxy-acetylene burning in a shipbreaking yard.

This case, which was twice admitted to Dr. John Gracie's wards at the Western Infirmary, Glasgow, was observed and treated by the author on both occasions.

Case History:

The patient, who had only been in Scotland for 6 weeks, had been employed in shipbreaking in a Clydeside yard during that time. When at this work he was exposed to lead fume resulting from his having to burn through old lead-painted steel plates with his lamp. When in Newcastle-upon-Tyne - where he had worked previously - he had never, as far as he knew, worked with lead to any great extent. During the 6 weeks he had been shipbreaking he had worked outside and did not wear a respirator.   He stated that there was considerable fume from the burning paint at times.   The company gave him a half pint of milk a day.   He had always been temperate.

On admission to hospital the man said that 'he had not felt right for a month' but that it was only for 5 days that he had felt really ill.   In that time he had felt sick and off his food and the bowels had been constipated.   He had suffered from vague abdominal pain, which had become much worse on the day before admission, causing him to be unable to work.   His doctor had been called in, and he found pulse and temperature normal;   he regarded the case as one of lead intoxication. The same night abdominal pain, which was persistent and 'all over the abdomen, returned.   It did not come on in spasms at that time.

He never had any sweating or shivering, but had complained of a
tingling sensation in his legs and a dull headache since the onset
of his illness.

His previous health had always been good, apart from sandfly
fever in Egypt in 1931.   He had never had malaria or dysentery.
Examination:

The patient was thin and rather pale, his face having
a somewhat anxious expression.   He appeared to be suffering from acute
pain.   His temperature was 99°F.

Cardiovascular system: His pulse was 64 per minute, regular and of
good quality, there being no thickening of the vessel wall.   Blood
pressure was 130/75.   Cardiac dullness was within normal limits and the
sounds were pure and of good tone.

Respiratory system: Respiration rate was 16 per minute.   No abnormal-
ities of the lungs were found.

Alimentary system: His teeth were in very poor condition, there being
many carious.   There was a definite lead line on the gums, but this
was rather faint.   The tongue was dry and covered with brownish fur
posteriorly.   The abdomen was thin and held rather rigid, not moving
to any great extent with respiration.   There was tenderness all over
the abdomen, more especially around the umbilicus, although this was
not very pronounced.   After a few moments the primary rigidity of
the abdomen relaxed.   No masses could be felt and there was no apparent
enlargement of the spleen or liver.   There was no visible peristalsis.
Rectal examination was negative.

Nervous System: The pupils were moderately dilated and equal, reacting to light and on accommodation. Ophthalmoscopic examination showed no abnormality. The function of other cranial nerves also seemed unimpaired. Arm, abdominal and leg reflexes were active and equal on both sides. Both plantar responses were flexor. There were no sensory defects. The grips of both hands were equal and there was no apparent weakness of the extensors of the forearm or leg.

Genito-urinary system: He had no complaints as regards micturition. The kidneys were not palpable. The urine was normal to the ordinary tests.

Special Investigations:

Blood count: Red blood cells 3,860,000
Haemoglobin 75 per cent
Colour index 0.96
White blood cells 9,200
Polymorphs. 82.5 (there being no
Schilling 'lift to the left')
Lymphocytes 14.0
Monocytes 3.5
Eosinophils nil
Basophils nil

Reticulocytes 6 per cent.

Leishman film: The red cells were well coloured and of normal size and shape. There were 2,500 stippled cells (with large, small and medium granules) per million erythrocytes. Frequent polychromatic cells were also seen.

Methylene blue film: This method showed 6,000 stippled cells per million erythrocytes, and polychromatic cells were also frequently observed.

Blood lead value: 109 μg. per 100 ml.

The urine contained 0.15 mg. Pb per litre.

Wassermann reaction: Negative.

van den Bergh: Faint positive indirect reaction.

Red cell fragility: within normal limits, haemolysis being complete in 0.45 per cent sodium chloride.

Blood urea: 46 mg. per 100 ml.

Treatment and progress:

On admission, after samples of blood had been taken for testing, he was given 10 ml. of 10 per cent calcium gluconate intravenously. He felt slightly better after this, although the pain again returned within an hour. A further 5 ml. was therefore given, and $\frac{1}{4}$ gr. morphine and 1/100 gr. atropine administered hypodermically. Hot cloths were applied to the abdomen. With this, he felt more comfortable.

He was given an enema, with good result, and also $\frac{2}{3}$ ii magnesium sulphate orally. Although he was disinclined to take food he was encouraged to take as much milk as possible. He subsequently remained comfortable but pain, which he said was more spasmodic than previously, returned the following morning. Another 5 ml. of 10 per cent calcium gluconate was injected intravenously and he felt more comfortable although he still complained of slight pain. In the evening another 5 ml. of calcium gluconate was injected intramuscularly. Since admission the temperature had never risen over 99°F. The pulse had never exceeded 80 per minute.

By the following day his symptoms had disappeared, but a high

calcium intake was maintained. His blood lead value was 85μg. per 100 ml. at this time. Blood films stained by Leishman's method showed 2,000 stippled cells per million erythrocytes. Retiouloocytes were 4.5 per cent. Two days later he demanded to leave hospital so that he could make arrangements to give up his work and return to England. He was therefore dismissed, with instructions to take at least two pints of milk and a teaspoonful of Epsom salts each day. When he got up he felt rather unsteady on his feet. The blue line on the gums was present as when admitted.

Re-admission: Two days later the man had to be re-admitted to hospital on account of return of the abdominal symptoms. There was slight tenderness round the umbilicus, but no rigidity. On this occasion the blood lead value was only 82μg. per 100 ml. The urine contained 0.025 mg. Pb per litre. The blood count was:

```
R.B.C.s    3,610,000
Hb.        72%
Colour index
W.B.C.s    9,600
```

Reticulocytes 2.5 per cent

Leishman film: 2,000 stippled cells per million reds.
Alkaline methylene blue film: 4,500 stippled cells per million reds.

The leucocytes showed no abnormality.

His temperature on re-admission was $99.6^{o}$and the pulse 76. He was given a further 10 ml. of 10 per cent calcium gluconate intravenously, together with a high calcium diet as previously. The next day he had again improved and wanted to leave hospital. When told that this was inadvisable he became very upset and burst into tears.

For two days, although he had no return of his symptoms (high calcium intake being maintained) he remained fretful and moody. His relatives in England had written to him to come home, and against all advice he left hospital to go there. He was given instructions as to diet and treatment and told to write to the author if symptoms returned. No communication from him has ever been received.

Remarks on the case:

This patient had only been exposed to lead for a comparatively short time. He was apparently very susceptible to lead, the presence of the lead line on the gums in itself indicating very excessive lead absorption. His own doctor had diagnosed him as lead poisoning, and his general appearance on admission suggested this. His pain was by no means typical, however, but the history, the faint lead line on his gums and his anaemia, associated with stippling of the erythrocytes, supported the diagnosis. He was a very neurotic man and it was difficult to assess to what extent he was suffering.

Biochemical results in this case were rather inconclusive, the lead content of blood and urine being slightly raised but not appreciably so.

His response to calcium therapy was not so dramatic as that of some cases the author has treated. He showed improvement following it, however, and it resulted in the blood lead value falling to almost normal limits. The recurrence of symptoms after his irregular dismissal from hospital was again corrected by similar treatment. On this occasion there was a slight polymorphonuclear leucocytosis and the temperature had risen to 99.6°; although the possibility of his having

an acute surgical emergency was considered his response to medical

treatment seemed in keeping with a diagnosis of lead poisoning.

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Case 4.

Lead poisoning arising from employment in a lead works.

A widower aged 66, whose occupation was that of a red lead
packer in a lead works, was sent by his doctor to the Outpatient
Department at the Western Infirmary, Glasgow, where he was seen by
the author and diagnosed as lead poisoning.   He had been seen previously
by another physician, who had arranged a barium meal X-ray examination.
The result was negative.   He was subsequently admitted to the wards
under the care of Professor J. W. McNee, who gave the author full
facilities for further observation, testing and treatment of the case.

Case History:

The man had not felt well for two years, although he had
been at work up till 5 weeks before admission.   For 10 years he had
worked in a lead works - either in the 'stacks' or else packing lead
oxide in drums, or other duties.   He wore a respirator "at times",
and had been regularly examined by the factory medical officer.   His
symptoms were those of weakness and lack of energy, and he had suffered
from several attacks of abdominal pain which he described as "colicky"
and which had become more severe during the past two years.   Five
weeks previous to admission he had such severe pain that he was forced
to give up work.   He had been drinking a good deal for years and had
not been taking a very satisfactory diet.   He said that he had
suffered from headache at times, but had never noticed any sensation
of numbness or pins and needles in his limbs.   His previous health
had always been good.

<u>Examination</u>:

Temperature and pulse, and respiration rates were normal.
The patient was a man of moderate build and of rather low intelligence.
He looked pale, his face having a somewhat ashen appearance.   There
was no oedema and he seemed fairly well nourished.

Cardiovascular system: The pulse was regular, the artery walls being
somewhat sclerosed.   The blood pressure on admission was 110/60.
The apex beat was 4 inches from mid-sternum in the 5th interspace.
The first heart sound was rather soft, although there were no definite
bruits at apex or base.

Respiratory system: No abnormality detected.

Alimentary system: His teeth were in very poor condition, and there
was an obvious blue line in the gums of both jaws.   This blue
colouration was noted to be most pronounced near the most carious teeth.
The tongue was dry and furred.   The abdomen was lax and free from pain
and tenderness at the time of examination.   The patient indicated the
site of the pain as just below the umbilicus.   There was no apparent
enlargement of liver or spleen.

Nervous System: Ophthalmoscopic examination showed no abnormality
apart from pallor, and no defects of the other cranial nerves were
noted.   There was a slight tremor of the outstretched hands.   His
grips were strong and equal.   The arm, abdominal and leg reflexes
were all present and equal.   The plantar responses were flexor.   No
sensory loss or weakness of the extensors was noted.

Special investigations:

>   Blood count: Red blood cells 2,930,000
>   Haemoglobin 47 per cent
>   Colour index 0.80
>   White blood cells 5,000
>   Polymorphs. 64.5
>   Lymphocytes 28.5
>   Monocytes   6.5
>   Eosinophils 0.5
>   Basophils   nil

Blood films stained by Leishman's method showed stippled red cells
(the granules being mostly large and medium in size) - 7,000 per
million erythrocytes.   There was obvious poikilocytosis and anisocytosis
and a few normoblasts (an occasional one being stippled); frequent
polychromatic cells were also noted.   Many of the red cells showed
'ring' staining.

>   Reticulocytes: 8.5 per cent.
>
>   Blood lead value: 166 μg. per 100 ml.
>
>   Blood urea: 49 mg. per 100 ml.
>
>   Wassermann reaction: Negative.

X-ray examination of hands and wrists showed some calcification of
vessels, but no abnormality apart from osteo-arthritic changes.

Treatment and progress:

> After a week without treatment and when on ordinary diet a
blood lead estimation was repeated. The result was 170 μg. per 100
ml.(see Chart 8).   He was then put on a high calcium diet and 5 ml.
10 per cent calcium gluconate injected intramuscularly, this being given
on alternate days for ten days.   At the end of this period, the blood
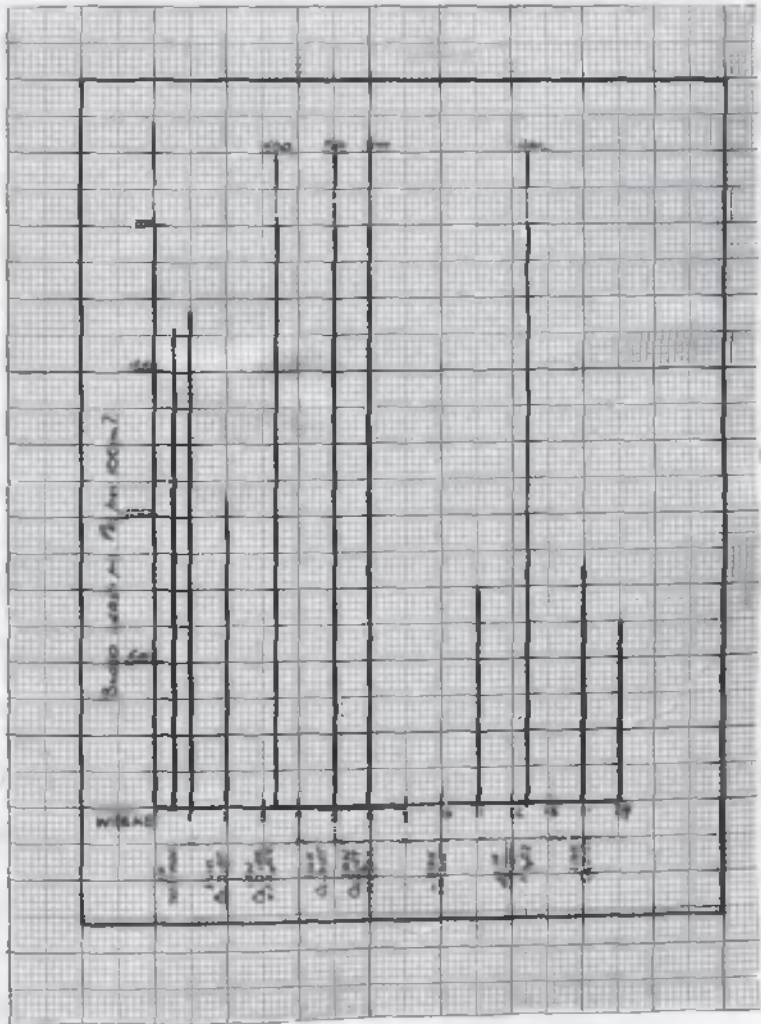lead value had fallen to 108 μg. per 100 ml. and the patient, who had

CHART 8.

never had any further attacks of pain, stated that he felt much better. Stippling of the erythrocytes was present at about the same level as when admitted.

He was then placed on a low calcium diet and ammonium chloride in doses of 1 g. q.i.d. was administered. There were no clinical ill-effects from this and in ten days the content of lead in the blood had risen to 500 μg. per 100 ml. Blood count figures at this time were:

```
R.B.C.s   3,060,000
Hb.       56 per cent
C.I.      0.93
W.B.C.s   6,000
```

Stippled cells (Leishman) 4,500 per million erythrocytes.

Reticulocytes 5.25 per cent.

A course of calcium injections together with a high calcium diet was then repeated, and at the end of eight days of this treatment the blood lead value had fallen to 248 μg. per 100 ml.

Repeating ammonium chloride therapy with a low calcium intake caused another rise in the blood lead level, the result being 307 μg. per 100 ml. at the end of a week of such treatment. He was subsequently placed on a high calcium intake, which was maintained. The patient was dismissed from hospital five weeks after admission, feeling very much better. His bowels were regular and his appetite was good. There had been no further abdominal symptoms. Although no haematinics had been prescribed his blood count had risen during this time to:

```
R.B.C.s   4,020,000
Hb.       70 per cent
C.I.      0.87
W.B.C.s   5,400
```

Leishman stained films showed occasional stippled cells with large, medium and small granules, but these were too infrequent to attempt to count.   A few polychromatic cells were noticed.   The red cells were more uniform in shape but still rather pale-staining.

No apparent ill-effects had occurred in association with the de-leading methods employed.   His blood pressure was now 130/85. His urine had always been normal to side-room tests.   The output had been between 36 and 54 ounces per day, and varied independently of treatment.   The blue line had, associated with efforts to improve his oral hygiene, become less apparent.   He was given instructions to take large amounts of milk and cheese daily, to take Epsom salts, to avoid alcohol and lead a regular life.

Eight days after discharge the patient was sent back to hospital by his doctor.   A few days after getting home he had developed swelling of the feet, which had become progressively worse. He was re-admitted.

Physical examination showed a moderate degree of oedema of the feet, ankles and lower parts of the legs.   He had never suffered from similar symptoms before.   Apart from the oedema there were no other alterations compared with his condition when discharged from hospital.   The heart sounds were soft but no bruits were heard. Blood pressure was 125/75, he had no varicose veins and the urine was normal.   The blood urea was 42 mg. per 100 ml.

He was treated with rest in bed and a high calcium intake for a week, when the blood lead value was 80μg. per 100 ml.   Subsequently

another course of ammonium chloride with low calcium intake was given for a week, no ill effects occurring. This caused the blood lead value to rise to 444μg. per 100 ml. By this time the oedema had subsided, he was put on a high calcium intake and allowed up. There was no return of symptoms and he was discharged with instructions as before. His blood lead value at the time of discharge had fallen to 90μg. per 100 ml. and his blood count was:

```
R.B.C.s    4,160,000
Hb.        78 per cent
C.I.       0.94
W.B.C.s    6,400
```

A very occasional stippled cell was seen after prolonged search. (Leishman).

Three months later he was re-examined and tested. Clinically he seemed satisfactory although his general appearance suggested that he had not been looking after himself very well. Blood pressure was 138/82. No blue line was visible on the gums and he had never suffered from any return of symptoms. There was no oedema. Blood count findings were:

```
R.B.C.s    4,240,000
Hb.        72 per cent
C.I.       0.85
W.B.C.s    6,400
```

No stippled cells could be seen on examination of a Leishman stained film.

The blood lead value was 72μg. per 100 ml.

He was put on an iron mixture, advised to have his teeth extracted and cautioned never to return to an occupation involving exposure to lead.

Remarks on the case:

This patient had developed chronic lead poisoning after many years of work in a dusty lead trade. The diagnosis was made clinically and the special investigations supported this opinion. By alternating high and low calcium intake the content of lead in the blood varied. He never showed any return of his old symptoms during this treatment, and at the end of two months there was considerable clinical improvement. The occurrence of temporary oedema of the legs was probably due to his going about too much after having been in bed. No organic cause could be found to account for this. The anaemic proved very stubborn to treatment with iron. No stippled cells were found four and a half months after his admission to hospital, and the lead line on his gums had also disappeared by this time.

Case 5.

Industrial lead poisoning due to the use of an oxy-acetylene lamp in a shipbreaking yard.

A man aged 64 was admitted to hospital, complaining of attacks of abdominal colic associated with general weakness and loss of colour.   For ten years he had been employed in a shipbreaking yard, regularly using an oxy-acetylene lamp to burn through old ship hulls. He frequently had been exposed to lead fume which was derived from paint on the plates through which he was burning.   Although he wore a respirator, he did not always use it and admitted to not being particular as regards this although he realised the danger involved. He had been supplied with half a pint of milk daily by his employers and had been examined regularly by a medical officer at the yard.   He stated that he took alcohol regularly and 'occasionally in excess'.

Case History:

Ever since he had started work in the above occupation he had not felt in perfect health.   He was easily tired and on several occasions previously he had lost time due to being off work 'on account' of his stomach'.   He had also been in hospital three years before, where he had been regarded as ? lead poisoning.   He returned to work, however, and although he felt better for a year or so abdominal pain, anorexia and constipation returned, and he was then admitted to hospital. He stated that in the three weeks before admission - during which time he had been at home - 'life hadn't been worth living', abdominal pain, constipation, weakness and giddiness being very severe.   He had tried to get his bowels regular with salts.

Examination:

He was a thin, sparsely-built man with a somewhat drawn expression and a somewhat greyish pallor of the face; his mucous membranes were pale. His pulse was regular and his heart sounds soft. Blood pressure was 135/95. There was no evidence of arterio-sclerosis or oedema. His chest was rather flat but no signs of disease were found in the lungs. The abdomen was rather thin but was free from pain and tenderness at the time of examination (5 days after admission). His tongue was rather dry and his teeth artificial. The buccal mucosae showed no abnormality apart from pallor. Examination of the nervous system revealed no evidence of organic disease, reflexes and sensation being normal and the power of the extensors and grips being equal and satisfactory.

Special investigations:

Blood count: Red blood cells 3,040,000
Haemoglobin 56 per cent
Colour index 0.95
White blood cells 6,200
Polymorphs. 71.5
Lymphocytes 22.5
Monocytes 5.5
Eosinophils 0.5
Basophils nil

Films stained by Leishman's method showed stippling of the erythrocytes (5,000 per million being so affected). The granules in many of these cells were large. There was a marked degree of variation in size and shape of the red cells but most of them were well coloured. No nucleated forms were seen.

Blood lead value: 222 μg. per 100 ml.

By the ordinary side-room tests the urine was normal.

He had been on ordinary light diet since admission.

Further observation of this case was not able to be arranged.

Remarks on the case:

The history, and clinical, haematological and biochemical findings all pointed to chronic lead poisoning being the diagnosis in this case.   The cause of poisoning was lead fume.   There was no evidence of any nervous or renal damage.   If, as he said, he had suffered from plumbism three years' previously he should never have returned to an occupation involving lead risk.

Case 6.

Industrial lead poisoning and chronic nephritis in a patient who was an electric accumulator worker.

A male aged 62, of large build, was admitted to hospital suffering from breathlessness, headache and swelling of the feet.   He had suffered from chronic kidney disease for about 10 years.   His employment was that of a lead burner in an electric accumulator works, and he had been exposed to lead in industry one way and another for about 15 years.   He had always been a heavy drinker and, although he had suffered from occasional mild abdominal colic for some time, these attacks had become worse in the past year.   About a year before that he had noticed a weakness in the right arm, but this had cleared up in a few months.

Examination:

The patient, when seen by the author, was in the last stages of cardiac defeat and consequently a detailed examination was impossible, and the information he could give about himself was not too satisfactory.

There was marked dyspnoea and oedema of legs, loins and arms. His face was bloated and cyanosed.   The mucous membranes were very pale.   The pulse was 84 per minute and very irregular.   There was marked thickening of the artery walls.   Blood pressure was 210/130. Heart sounds were heard with difficulty owing to numerous rales in the lungs.   There was no apparent pericarditis.   The bases of both lungs showed signs of congestion.

There was a well-defined blue line on the gum margins round his remaining teeth.   The abdomen was distended and the liver tender.

The scrotum was oedematous.

Special investigations:

Blood count:

	Red blood cells	3,420,000
	Haemoglobin	60 per cent
	Colour index	0.88
	White blood cells	5,800
	Polymorphs.	78.5
	Lymphocytes	18.0
	Monocytes	3.5
	Eosinophils	nil
	Basophils	nil

Films stained by Leishman's method showed marked stippling of the

erythrocytes (6,000 per million) and also frequent polychromatic cells.

The granules of the stippled cells were mostly of medium size, although

some were large.   Many of the red cells were hypochromic and

anisocytosis and poikilocytosis was fairly marked.

Blood lead value: 174 μg. per 100 ml.

Wassermann reaction: Negative.

Blood urea: 220 mg. per 100 ml.

The urine contained abundant albumin and granular casts.

The man died shortly after the above examination.   No

autopsy was permitted.

Remarks on the case:

The late results of the action of lead are shown by this case.

Whether or not the nephritis had primarily been caused by the action

of lead is a debatable point.   The same can be said with regard to

the alcohol.   These factors, however, had probably played an important

part in precipitating his death.   Diagnosis was made clinically and

confirmed by the raised blood lead value and the presence of appreciable

numbers of stippled cells in blood films.　Lead fume, for the most part, seemed to have accounted for the poisoning in this case.

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Case 7.

Increased lead absorption following painting and paint mixing.

A male aged 25 was seen by Dr. D. Riddell Campbell at the Outpatient Department of the Western Infirmary, Glasgow, and was referred to the author.   In his occupation, which was that of a painter, the man had been exposed to dust containing lead.   He had regularly mixed lead paints, and in the mixing room his duties included the laying of dust sheets and the sweeping of floors.   He never wore a respirator.

Case History:

He complained of headache and being off his food for a month. His bowels had been costive and in addition he had a 'numb feeling' in his right leg and foot.

Examination:

He was a thin nervous youth with rather a sallow complexion. There was no lead line present on the gums.   General examination was negative, although the right knee jerk was somewhat sluggish.   There was no evidence of foot drop.

Special Investigations:

Blood count: Red blood cells 4,600,000
              Haemoglobin 80 per cent
              Colour index
              White blood cells 7,500

              Reticulocytes 1.5 per cent.

Blood lead value: 200 μg. per 100 ml.

Wassermann reaction: Negative.

His urine was normal by the ordinary tests.

Treatment and Progress:

He was put on a high calcium intake for 3 weeks, this being given in the form of 2 pints of milk and gr. 90 calcium lactate daily. At the end of this time his blood lead value had fallen to 65μg. per 100 ml and after another 10 days of similar treatment it was 47μg. per 100 ml. (see Chart 9).   By this time marked general improvement was shown, although he still complained of occasional 'cramps' in his right leg.

Remarks on the case:

Although from the evidence obtained, this case could not be regarded by the author as lead poisoning, the general examination and history suggested that lead possibly accounted for some of his obscure symptoms.   The raised blood lead value of 200μg. per 100 ml. was in keeping with this view, and, with a raised calcium intake, the blood lead value fell to within normal limits.   There was some clinical improvement associated with this, but as clinical findings pointing to lead poisoning had been very indefinite in the first place, it was decided to designate this case "increased lead absorption" rather than lead poisoning in the accepted sense.   Such a case presents certain difficulties as regards medical certification of the illness;   this point is discussed elsewhere.
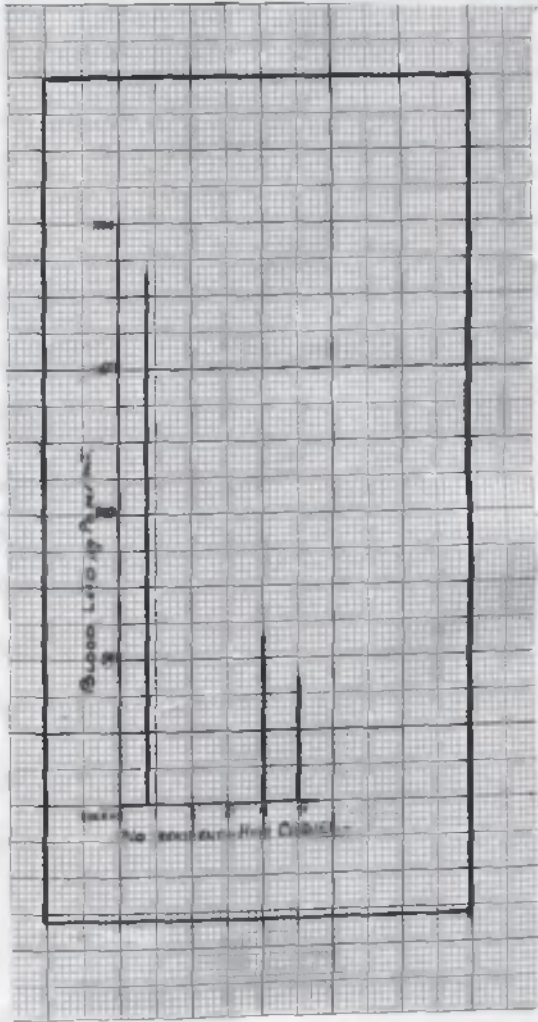
BLOOD UREA IN MGMS PER

No tourniquet-Red Cubicle

CHART 9.

Case 8.

Increased lead absorption due to occupational exposure
to lead paint.

A red leader, aged 56, was admitted to the Southern General Hospital, Glasgow, under the care of Dr. W. R. Snodgrass, who gave the author facilities for testing, observation and treatment of the case.

Case History:

The man had been in good health all his life until three weeks before admission, when he began to 'feel useless' and complained of frequent headaches and dizziness. He stated that he felt his arms rather weak. There had never been any other symptoms and his bowels had always been regular.

He had worked amongst lead paint for 30 years, but realised the risk and had always been very particular when working with it. He had frequently done paint-mixing during his life, and had also done 'dry rubbing down'. There had been no increase in his exposure to lead as far as he knew. He very rarely took alcohol.

Examination:

The man was well built and of satisfactory colour. General examination failed to reveal any signs of organic disease. Heart sounds were of good tone and the blood pressure 120/75. The fundi were normal, as were reflexes and muscular power. He was edentulous and the buccal mucosa showed no abnormality.

Special investigations:

Blood count: Red blood cells 4,300,000
Haemoglobin 80 per cent
Colour index 0.90
White blood cells 6,000

Polymorphs. 59.0
Lymphocytes 18.5
Monocytes 11.0
Eosinophils 1.0
Basophils 0.5

Films stained by Leishman's method showed the red cells to be normochromic with slight variation in size. No stippling was found.

Blood lead value: 149 μg. per 100 ml.

Blood urea: 26 mg. per 100 ml.

Wassermann reaction: Negative.

The urine was normal by the ordinary tests.

Treatment and progress:

He was placed on a high calcium diet and 5 cc. 10 per cent calcium gluconate were given, on alternate days for 10 days. At the end of this time he stated he felt very much better and was anxious to get out of hospital. His blood lead value following this treatment had fallen to 54 μg. per 100 ml. Further examination of blood films was again negative for the presence of stippled cells.

Remarks on the case:

This man had been exposed to lead paint for many years. The symptoms he presented might have been due to hyperpiesis, but this diagnosis was subsequently excluded. The raised blood lead value which, with high calcium therapy was lowered to normal limits pointed to increased absorption of lead. The fact that clinical improvement occurred with this may have been due, to some extent, to his resting in bed. However, the fact that it did occur associated with efforts to remove lead from the circulation strongly suggested that increased

lead absorption might well have accounted for his illness.   The
author considered it likely that this had occurred, although the
man was by no means 'poisoned' in the ordinary sense.

———————

Case 9.

Increased lead absorption occurring due to paint grinding.

A male aged 33 was admitted to hospital complaining of general weakness and a numb feeling in his arms. He had been employed as a paint grinder for $2\frac{1}{2}$ years and before that had, when working as a general labourer in the United States, occasionally mixed paints. Although when grinding paint he had worn a respirator, he didn't consider it very effective. He had been regularly examined by the 'factory doctor' when at work. Although care was taken to avoid lead dust as much as possible he said that a certain amount of it was unavoidable in his occupation. He did not drink much milk and rarely took alcohol. He had never suffered from any serious illness in the past.

Case History: For 5 months before admission he had noticed he was progressively losing interest in things and thought there 'wasn't the same power in his arms and legs'. He had suffered from occasional headaches and a numb sensation in his arms. He had never had any abdominal pain although he had always a tendency to constipation.

Examination: He was a thin neurotic man who made the most of his troubles. Examination failed to reveal any clinical signs of plumbism. Although several teeth were carious there was no lead line on the gums. The grip of the right hand was not, perhaps, as good as that of the left, although this was not marked, and reflexes and sensory power were normal. There was no evidence of muscular atrophy. His blood pressure was 126/85, and no abnormalities were found in the cardio-vascular, respiratory or genito-urinary systems.

<u>Special investigations on admission</u>:

Blood count: Red blood cells 4,100,000
                             Haemoglobin 83 per cent
                             Colour index 1.0 (approx.)
                             White blood cells 7,400
                             Polymorphs. 68.0
                             Lymphocytes 27.0
                             Monocytes   5.0
                             Eosinophils   nil
                             Basophils   nil

Examination of blood films stained by Leishman's method failed to detect any stippled erythrocytes.   The red cells appeared of average size and colour.

Blood lead value: 184 μg. per 100 ml.

Wassermann reaction: Negative.

The urine contained 0.10 mg. Pb per litre.   The ordinary side-room tests were negative.

<u>Treatment and progress</u>:

After being on a high calcium diet together with calcium lactate gr xv q.i.d. for 3 weeks the man felt much better.   He seemed brighter, although still somewhat introspective.   His blood lead value had fallen to 64 μg. per 100 ml. and another week of similar treatment caused a further fall to 45 μg. per 100 ml.

After being at home for 6 weeks, where he took extra milk he was re-tested and the blood lead value found to be 102 μg. per 100 ml. His urine contained .04 mg. per litre at this time.   No stippling had been seen in blood films stained by Leishman's method at any time. Clinically, he had improved with the dietetic treatment although he still felt tired towards the end of the day.   Large doses of ferri

et ammon. citrate were prescribed.   He was advised to change his
employment and avoid further exposure to lead.

Remarks on the case:

In this case there was chemical evidence of increased lead
absorption, but as nothing definitely indicative of lead intoxication
was found clinically - and no stippled cells being found in blood
films - he was designated "increased lead absorption".   His response
to high calcium intake was, on the whole, satisfactory.

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et anis parragot fordin fastidia vicur

Horace (c. 4 B.C.)

by Conington (1873):

"Does press water strain your pipes of lead
than that which rippled down the brooklet's bed
Drive Nature forth by force, she'll turn and rout
the false refinements that would keep her out.

PLUMBISM ARISING FROM

DRINKING WATER DELIVERED THROUGH LEAD PIPES.

"Purior in vicis aqua tendit rumpere plumbum
quam quae per pronum trepidat cum murmure vivum?
Naturam expelles furca, tamen usque recurret
et mala perrumpet furtim fastidia victrix."

Horace (c.25 B.C.)

Translated by Conington (1872):

"Does purer water strain your pipes of lead
than that which ripples down the brooklet's bed?
Drive Nature forth by force, she'll turn and rout
the false refinements that would keep her out."

Case 10.

Lead poisoning arising from a private water supply.

The symptoms of the case described were found attributable to lead present in drinking water coming from a spring and conveyed through a lead pipe.

Case History.

The patient, a farmer's wife aged 27, whose previous health had always been good, was admitted to hospital complaining of headache, nausea and vomiting. For eighteen months she had not felt well, being easily exhausted and suffering from attacks of vomiting, constipation and abdominal pain. A year before admission to hospital she had noticed 'her teeth and gums darkening' and had all her teeth extracted at that time, the dentist apparently noticing nothing abnormal with her gums. During the summer months before admission to hospital she noticed that her eyesight was failing and that her symptoms were becoming worse. She also complained of a sensation of numbness and tingling in her legs and arms. She stated that 'she hadn't the same grip when milking'.

Clinical Examination.

When the case came under the author's observation she had been in hospital for two weeks, being regarded in the first place as a possible case of intracranial neoplasm. The finding of stippled erythrocytes in blood films, however, had brought forward the question of lead poisoning. She had been treated with parenteral calcium

gluconate, and on account of the persistent vomiting a continuous drip rectal saline with glucose had been given.

On examination, she was found to be pale and showed some loss of weight. There was no cyanosis, jaundice, oedema or enlargement of superficial glands. Her temperature was normal and had been so since admission. The pulse was soft - 72 per minute - and the blood pressure 115/75. The heart sounds were pure and the lungs clear. The tongue was dry, the persistent vomiting having given rise to dehydration. The abdomen was lax and free from tenderness. There was no apparent enlargement of liver or spleen. The urinary output had varied from 16 to 30 ounces per day since admission, and catheterisation had been required occasionally. The urine had contained a trace of albumin at times.

The pupils were moderately dilated and equal, reacting as in health. There was a left external rectus palsy, present since childhood. Ophthalmoscopic examination revealed bi-lateral papilloedema with numerous flame-shaped haemorrhages and patches of retinitis in both fundi. The veins appeared congested. There was no limitation of the fields of vision. No evidence of involvement of other cranial nerves was discovered. The arm and abdominal reflexes, although sluggish, were present and equal. Knee and ankle jerks were active and equal and both plantar responses were flexor. No defects of sensation were noted. These findings were confirmed by Dr. J. B. Gaylor, neurologist at the Western Infirmary, Glasgow.

Special Investigations.

Blood examination:

> Haemoglobin 59%
> Red blood corpuscles 3,120,000 per c.mm.
> White blood corpuscles 6,800 per c.mm.
> Colour index 0.95

Films stained by Leishman's method showed the majority of the red cells to be normochromic, others being somewhat pale with some degree of anisocytosis and poikilocytosis. Stippled red cells were frequently seen (18,000 per million erythrocytes) as were polychromatic cells. An occasional normoblast was found.

Differential white cell count:

> Basophils nil
> Eosinophils 0.5%
> Neutrophil granulocytes (mature) 64.5%
> Lymphocytes 26%
> Monocytes 9%

Intravitally stained films, counterstained by Leishman's method, showed a reticulocytosis of 9 per cent. A few reticulated normoblasts were noted.

Red cell fragility: Within normal limits, haemolysis being complete in 0.45 per cent sodium chloride.

Blood urea: 49 mgm. per 100 ml.

Blood Wassermann reaction: Negative.

Blood lead estimation: 149 μg. per 100 ml.
(N.B. taken after calcium
therapy for some days)

Treatment and Progress.

In spite of calcium therapy, given on account of the vomiting in the form of calcium gluconate (10 ml. of 5 per cent solution intramuscularly), which was associated with a fall in the blood lead content to within normal limits, the patient's condition became progressively worse. Vomiting and generalised headaches persisted. There was no abdominal pain at this time. Vision became further impaired and she began to show mental changes, being very confused and suffering from hallucinations of sight and hearing. She was very noisy and talked absolute nonsense. There were no convulsions.

On stopping calcium therapy the blood lead had risen to 185 and then to 215 μg. per 100 ml. The urinary output remained low and contained a trace of albumin at times. No casts or blood cells were found. (See Chart 10).

A lumbar puncture showed the cerebro-spinal fluid to be under increased pressure. The fluid was clear and the Wassermann reaction negative. Further tests on the cerebro-spinal fluid were, unfortunately, not obtained.

She seemed slightly improved after the lumbar puncture, being more rational. Further calcium therapy had depressed the blood lead to 96 μg. per 100 ml. This clinical improvement was only temporary, however; her condition became much worse and she passed into coma. She died after being in hospital eleven weeks. She had been afebrile throughout the illness until just before death. Blood count figures two days before death were:

CHART 10.

> Haemoglobin 46%
> Red blood corpuscles 2,860,000
> White blood corpuscles 4,600
> Colour index 0.8
> Stippled erythrocytes 7,000 per million
> Numerous polychrome cells.
> Reticulocytes 7%

The blood urea had risen to 90 mgm. per 100 ml.

A post mortem examination was carried out by the author and Dr. A. E. Struthers on the day of the patient's death.   Generalised pallor of the tissues was found but no macroscopic evidence of organic disease was demonstrable.   The meninges appeared normal, there being no evidence of oedema of the brain or flattening of the convolutions. Sections of the brain and inspection of the calvarium showed no evidence of tumour or haemorrhage.   The heart was pale but otherwise healthy; the lungs appeared normal.   Liver, kidneys and spleen showed no enlargement or obvious signs of disease, and apart from a few faecoliths and several slightly enlarged mesenteric glands, the abdominal viscera were all normal.

Portions of liver, kidney, spleen, brain meninges and bone were taken for histological and chemical examination.

Histological findings (reported by Dr. A. C. Lendrum, Assistant Pathologist, Western Infirmary, Glasgow):

"The tissues are rather autolysed.   The kidneys show a definite slight increase of the interstitial tissue but any arterial changes seen are no more than might be found normally at this age.   There is a fine, almost diffuse, deposit of haemosiderin (as shown by the prussian blue reaction) in the cells of some of the convoluted tubules.

The liver shows central degenerative changes and the presence of considerable haemosiderin as granules in the cells of the portal zones.   The cerebral cortex shows no definite evidence of degeneration in the nerve cells, and there is no sign of endothelial proliferation in the capillaries.   In the tissue beside many of the small vessels there are one or two large phagocytes containing golden brown pigment; this does not show the characteristic crystalline form of haematoidin but it is negative to the prussian blue reaction.   A few small round cells are seen, less definitely related to the blood vessels, in which the cytoplasm shows an extremely fine granular blue staining with the iron reaction."

Tissues were also analysed for lead content, and the following table shows the results as compared with the average lead content of tissues found at postmortem by Tompsett (1936).

Tissue	Normal (mean or limits)	From case
Brain	0.5 mgm. per kgm.	3.08 mgm. per kgm.
Rib	8.55 mgm. per kgm.	52.08 mgm. per kgm.
Femur	18.2-108.3 mgm. per kgm.	52.10 mgm. per kgm.
Tibia	15.3-96.5 mgm. per kgm.	53.3 mgm. per kgm.
Kidney	1.75 mgm. per kgm.	4.62 mgm. per kgm.
Liver	1.73 mgm. per kgm.	7.14 mgm. per kgm.

Source of the poisoning.

The patient, when questioned, had stated that she had never worked amongst lead, and had not been taking any medicine or pills apart from those prescribed by her own doctor.

On visiting the farm where she had lived for two years it was discovered that the water supply came from a spring and that it was conveyed from a collecting tank to the house through a pipe three quarters of a mile long.

Samples of water taken from the cold tap gave the following results on testing for lead:

	Dithizone method	Sulphide method
Sample 1.	6.25 mg. Pb. per litre	6.0 mg. Pb. per litre
2.	8.0 " " " "	-
3.	7.3 " " " "	8.0 " " " "
4.	5.7 " " " "	6.0 " " " "

Tea made from sample 3 and tested by the dithizone method showed a lead content of 6.25 mg. per litre.

These samples were taken at different times over a period of ten days, and under varied weather conditions. All samples, without concentration, showed the presence of lead on testing qualitatively by adding 3 ml. of glacial acetic acid and 5 drops of potassium chromate.

The water was delivered from the spring to the collecting tank through an earthenware pipe. Samples of water from the collecting tank showed on analysis:

pH 6.3 (estimated with a Lovibond tintometer
using B.D.H. Universal Indicator).
No trace of lead.
Hardness 4.5 degrees (3.6 degrees being permanent).

Water taken from the collecting tank and tested for plumbo-
solvency in standard lead pipes gave the following results:

	Dithizone method (mg. Pb. per litre)	Sulphide method (mg. Pb. per litre)
After 24 hours contact (stagnant):	24	25
After 48 hours contact (stagnant):	36	36

Thus the source of contamination was proved to be the service
pipe.   Removal of the pipe showed that it was composed of lead
throughout the three quarters of a mile of its length, except for
some small lengths of copper piping, where it had been repaired.
Following these investigations, which were reported to the owner of
the property, an iron pipe lined with a bituminous preparation was
laid in its place and pipes of similar construction were laid in the
house.

Examination of others drinking the water.

On discovering this high content of lead in the drinking
water immediate steps were taken to question and examine other persons dr
drinking the supply - the patient's husband and two children.

The farmer, aged 34, looked rather pale and was found to have
an ill-defined although definite "lead line" on his gums.   He had been
constipated occasionally and had suffered from bouts of "indigestion"
although never from colic.   Apart from the pallor and blue line there
were no clinical signs of disease.

Blood examination: Red blood cells 3,680,000
                       Haemoglobin 62 per cent
                       Colour index 0.85
                       White blood cells 4,600

Blood film stained by Leishman's method.   Red cells were mostly

hypochromic;   8,000 per million were stippled.   Polychromatic cells

were also seen.   Leucocytes were normal.   Reticulocytes 6 per cent.

Blood lead value: 143μg. per 100 ml.

Arrangements were made for the household to obtain pure

water whilst a new pipe was being laid.   He was put on an increased

calcium intake (2 pints of milk a day and calcium lactate gr. xLv

daily) together with oral iron.   With this treatment the blood lead

value fell to 88μg. per 100 ml. in a month and two months later

was 38 g. per 100 ml.   By this time punctate basophilia and

reticulocytosis had disappeared.   Another month later the lead content

of the blood was 75μg. per 100 ml., and the blood count had improved

to:
                       Red blood cells 4,930,000
                       Haemoglobin 90 per cent
                       Colour index 0.9
                       White blood cells 7,800

Clinically, the blue line was found to have practically disappeared.

He stated that he felt very well.

Female child aged 10.

She had never suffered from any complaints.   Clinical

examination revealed no gross abnormality.   Teeth and gums were normal.

The conjunctival mucous membranes were rather pale.   Bowels had been

costive at times.

Blood examination: Red blood cells 3,240,000
                       Haemoglobin 62 per cent
                       Colour index 1 (approx).
                       White blood cells 5,200

Films (Leishman) showed stippled erythrocytes in the proportion of approximately 1,000 per million red cells. Polychromatic cells were fairly frequently seen. Reticulocytes 5.5 per cent. Blood lead value 95 μg. per 100 ml.

With an increased calcium intake the blood lead fell in a month to 57 μg. per 100 ml. At this time occasional stippled cells were seen in the Leishman stained blood film. Two months later the blood lead value was 84 μg. per 100 ml. and treatment with iron had improved the blood count to:

            Red blood cells 4,740,000
            Haemoglobin 85 per cent
            Colour index 0.9
            White blood cells 7,000

She felt in normal health.

Male child aged 8.

He had no history of any complaints apart from occasional constipation. He was well nourished and there was no "lead line" on the gums. His conjunctival mucous membranes were rather pale.

Blood examination: Red blood cells 3,510,000
            Haemoglobin 66 per cent
            Colour index 0.9
            White blood cells 6,600

Blood films showed the red cells to be normochromic. Occasional stippled cells, which were too infrequent to count, and polychromatic cells were seen. Reticulocytes 3.5 per cent. Blood lead value 109 μg. per 100 ml.

With a month's increased calcium intake the blood lead fell to 80 g. per 100 ml. and no stippled cells could be found at that time by the Leishman stained blood films. At the end of a further two

months the blood lead value was 38 μ g. per 100 ml. and, following
iron therapy, blood count figures were:

> Red blood cells 4,670,000
> Haemoglobin 92%
> Colour index 0.9
> White blood cells 5,200

Leishman stained blood films showed the red cells to be normochromic.
There were no stippled erythrocytes.

The child looked and felt more healthy than previously.

A farm servant was the only other person who occasionally
drank the water.   She had no symptoms or signs suggestive of
plumbism.   She would not submit to a blood test.

There was no history of sickness amongst the farm stock.

As the pipe had been laid for about eight years, enquiries
with regard to others who had lived in the farm previously and who had
drunk the same water supply failed to reveal the history of any
illness.

Remarks on the case:

As lead poisoning arising from water supplies and lead
encephalopathy are now both uncommon the above record presents several
interesting points:

(1)   The woman's illness presented a problem in diagnosis.
She had primarily been considered a case of cerebral tumour.

(2)   The diagnosis of lead poisoning was first suggested
by finding stippled erythrocytes in stained blood films.

(3)   A raised blood lead value was further evidence of
plumbism.

(4)   The clinical symptoms and signs - papilloedema, retinitis, partial blindness and diplopia, mental confusion, hallucinations, vomiting, oliguria and increased pressure of the cerebro-spinal fluid - were all in keeping with lead encephalopathy (Gowers, 1888; Oliver, 1914).

(5)   Although the blood urea had risen just before death, presumably due to dehydration, the urine had been normal to the ordinary tests throughout.   There had been no clinical evidence of nephritis.

(6)   Clinically, she became progressively worse in spite of treatment which lowered the blood lead value.   On discontinuing calcium injections it rose again before death.

(7)   Increased amounts of lead were found in her tissues -- especially the bones - at post mortem.   The highest amounts were found in the ribs.   Cortical bone did not contain unduly large amounts of lead.

(8)   No very definite histological changes were noted in the tissues after death.

(9)   The husband and children, who although perhaps not taking so much water as the patient, all showed evidence of increased lead absorption.   All had anaemia, with stippled cells in the blood. They had also raised blood lead values.   The man showed a blue line on the gums.

(10)   As far as the author could discover, other persons drinking the water from the pipe had never had any acute symptoms.

(11)   These cases show particularly well the tendency
to individual susceptibility causing ill effects following increased
lead absorption.   One of the four persons died; the others, with
treatment, recovered satisfactorily.   Ingleson (1934) comments on
the frequency with which one or two members of a household are affected by
drinking water containing excessive amounts of lead.   Had increased
lead absorption been maintained there is no doubt that in time they
would most probably all have suffered from severe plumbism.

(12)   The farm water supply came from a spring and the
water was soft and of slightly acid reaction at the times of testing.
Its rapid action on lead pipes was shown by the plumbosolvency tests
carried out.

Lead Poisoning from Water Supplies.

The question of risk of lead poisoning arising from water
supplies can be reconsidered briefly at this point.

Although it has been recognised since Roman times that water
delivered through lead pipe can be contaminated by the metal it is
not widely recognised that practically every water delivered through
lead pipes contains traces of lead even though, as in most cases, only
the house pipes are constructed of lead (Ingleson, 1934).   Soft acid
waters from peaty sources have long been recognised as being the most
plumbosolvent, but as Beale and Suckling (1931) and Ingleson have

pointed out, it is not these waters only that have this property.
Factors such as electrolytic action and chloride and oxygen content
can also increase the plumbosolvent action of water.   Waters of
high phosphate content have as a rule only a very slightly solvent
action on lead pipes (Currie, 1936).

As a general rule water lying stagnant in lead house pipes
contains most lead, although, as Ingleson points out, this is not
invariably the case.   Several samples of water taken from house
taps in the Glasgow area were tested for lead by the author, using
the dithizone technique employed when dealing with the heavily
contaminated samples previously mentioned.   Results are recorded in
Table XIII.   Those samples obtained after the water had been lying
stagnant overnight always contained higher amounts of lead than those
analysed after flushing the pipes.

As already stated, opinions vary greatly as to what quantity
of lead in water should be regarded as poisonous;   such figures are of
necessity given as the result of negative rather than positive evidence.
In the author's opinion, any supply constantly containing more than
0.15 mg. per litre should not only be "regarded with suspicion" as
suggested by some writers, but should be corrected.

TABLE XIII.

Samples of Glasgow tap water tested for lead.

No.	Sample District	First water withdrawn from cold tap in the morning. mg. Pb per litre	Sample obtained after frequent use of tap during day, and after running for 5 minutes. mg. Pb per litre
1.	Kelvinside	0.08	0.041
2.	Kelvinside	0.105	0.022
3.	Springburn	0.111	0.029
4.	Bearsden	0.133	0.034
5.	Riddrie	0.09	0.024
6.	Clarkston	0.118	-
7.	Springburn	0.079	0.019

Six control samples using glass distilled water were all negative when tested for the presence of lead.

LEAD POISONING DUE TO

LEAD ACETATE TAKEN AS AN ABORTIFACIENT.

"Every woman being with child, who
with intent to procure her own
miscarriage shall administer to
herself any poison or other noxious
thing........shall be guilty of
a felony........"

Offences Against the Person Act
1861. Sect. 58.

Case 11.

Poisoning due to lead taken as an abortifacient.

Poisoning by lead for purposes of criminal abortion has
frequently been reported in the past, e.g. in the Nottingham case (1906).
Due to legislation, as already pointed out, it is now more difficult for
persons to purchase lead preparations.   Abortion by this means, however,
is still practised and the author, in conversations with general
practitioners working in various social spheres, has heard that it is
more common at the present time than is generally thought, especially
in the north and midlands of England.

The preparation usually taken is diachylon (emplastrum
plumbi) in the form of pills.   Instances in which a soluble salt has
been employed appear to be less common.   The following case, in which
lead acetate was ingested to cause abortion, was admitted to the
County of Lanark Infectious Diseases Hospital, Motherwell, having been
notified as 'puerperal pyrexia'.

Case History.

A married woman, aged 25, whose previous health had always
been good, was admitted to hospital complaining of general weakness, loss
of colour, "pains in the bones" and attacks of severe abdominal colic
associated with obstinate constipation.   Her symptoms had lasted for six
weeks, and in that time had become progressively worse.   She also
complained of a foul taste in her mouth and at times felt a sensation of
numbness in her hands and feet.   She stated that she had been pregnant
for two months, but had had a complete abortion two weeks before admission
to hospital.   She admitted having taken "medicine" given to her "by a

friend" during the second month of the pregnancy, and it was subsequently found that this "medicine" was a solution of acetate of lead made up by adding about 70 grains of lead acetate to a pint of boiling water.   In all she swallowed $1\frac{3}{4}$ pints of the solution over a period of a month, $\frac{1}{2}$ oz. being taken three times a day during the first, second and fourth weeks.   As lead acetate is readily soluble in water and as the bottle was well shaken before taking a dose, it may be assumed that gr. 1.75 were taken three times a day and that, in all, about gr. 110 were ingested.

The following shows the history of symptoms and signs in the first week in relationship to the dose taken:

	Symptoms and signs.	Amount of lead acetate taken to date.
3rd day.	Felt sick. Anorexia. Pains in the stomach.	gr. 12
4th day.	Occasional vomiting. Constipation and griping pains. "Teeth started to darken" (?)	gr. 16
7th day.	Colic, sickness and vomiting worse. Pallor and "lead line" on gums noticed by husband.	gr. 37

The earlier symptoms are more significant, since, with vomiting, which started in the middle of the first week of ingestion of the drug, much of the lead acetate swallowed must have been returned in the vomitus.   In spite of the severe symptoms of poisoning the patient stated that she carried on with regular doses up to the time of the abortion.   In the second week constipation, colic, pallor and vomiting became worse, and in the third week, although no lead was taken she felt so ill she could hardly stand.   Abortion occurred at the end of

the fourth week, when about gr. 110 of lead acetate had been taken.
By this time she was completely exhausted, with frequent vomiting and
colic which she described as agonising, and "arising from around the
navel". It came on in spasms, lasting two to five minutes, sometimes
every fifteen minutes or so. These symptoms persisted until admission
to hospital.

Clinical Examination.

On admission the patient was very weak and exhausted. She
was emaciated, pallor of the skin and mucous membranes was pronounced,
and the face had an ashen colour. There was a very obvious "lead line"
round the gums, and a blue-grey discoloration of several carious teeth
was noted. The tongue was dry and coated with a grey metallic fur.
Slight tenderness was present in the epigastrium. There was a tachy-
cardia with a V.S. murmur at the apex and base of the heart. Blood
pressure was 125/85 mm. Hg. The sclerotics were of a bluish tinge.
Ophthalmoscopic examination showed no obvious changes apart from general
pallor of the fundi. Knee-jerks and supinator jerks gave a very feeble
response, but apart from these signs and the history of occasional
numbness in the hands and feet there were no signs of derangement of the
nervous system. At the time of examination there were no clinical signs
of recent pregnancy or abortion. By the ordinary tests the urine was
normal.

Blood Examination.

The following results were found on examination of the blood:

        Red blood cells 2,270,000
        Haemoglobin 48 per cent
        Color index 1.09
        White blood cells 6,800

Reticulocytes 12 per cent.   In blood films stained by Leishman's method punctate basophilia, mostly of a coarse type, was observed in 2.5 per cent of the erythrocytes - i.e. 56,750 stippled cells per c.mm. and macrocytes and polychromatic erythrocytes were also seen frequently. There was considerable anisocytosis and a few normoblasts were present. A differential leucocyte count showed the following:

                Polymorphonuclears 59 per cent
                Eosinophils   0.5   "   "
                Basophils   nil
                Lymphocytes   32   "   "
                Monocytes   8.5   "   "

There was no increase in blood fragility.   The van den Bergh reaction gave a positive indirect result.   Wassermann reaction negative.   A blood-lead estimation was not carried out on admission to hospital, but several estimations were performed later (vide infra).

Treatment and Progress.

Salines and enemata were given and the patient was put on a high calcium intake.   This treatment, which was well tolerated, quickly relieved the colics and as early as the third day clinical improvement was apparent.   Later, when acute symptoms had subsided, the patient was put on a low calcium intake in order to establish a negative calcium balance and on the fourth day of this diet a course of parenteral parathyroid extract was started.   Throughout the course of injections serum-calcium estimations were made as a control of treatment, as were blood-lead estimations (see Table XIV). The parathyroid preparation used was Parathormone (Lilly) given intramuscularly.   Smaller doses than those usually employed were used, owing to the acute symptoms having been

fairly recent.

      In all, 240 units of parathormone were given in the first course, with a resultant rise in both serum calcium and blood lead values (see Table XIV). That the dose had caused a toxic amount of lead to have been withdrawn from the bones was shown by the fact that the patient had a return of colic at the end of the course. This was quickly and dramatically relieved by an intravenous injection of 10 ml. 10 per cent calcium gluconate - the pain had practically disappeared by the time the injection was complete - and a subsequent high calcium diet.

Table XIV.

Details of first course of parathormone

Day	Units of parathormone	Serum calcium mg. per 100 ml.	Blood lead value μ g. per 100 ml.
1	20	8.8	200
		(before injection)	
2	20	9.0	-
3	20	-	-
4	40	9.5	-
6	40	-	-
7	40	10.3	-
9	40	-	-
10	20	-	-
11	-	11.9	230

Following the course of parathormone the patient showed considerable clinical improvement, feeling much stronger. The anaemia proved stubborn to treatment with iron alone, given orally, and although no sharp reticulocyte response was noticed combined treatment with intramuscular liver extract in the form of Campolon (Bayer), 4 ml. twice weekly and oral iron in the form of Colliron (Evans), one drachm three times daily caused a gradual improvement in the blood count.

The patient having been on a high calcium intake for three weeks after the first course of parathormone, a negative calcium balance was again established and another course of 240 units was given. This was well tolerated, the blood lead value rising from 200 to 235μg. per 100 ml. (see Chart 11). There was only a slight rise in serum calcium on this occasion, namely from 8.8 to 9.8 mg. per 100 ml.

Clinical improvement again followed this second course and the patient was subsequently placed on a high calcium intake. A progressive fall in the blood lead value was associated with this treatment (see Chart 11). By this time, over two months after admission, the patient was well enough to get up for a short time each day. She was gaining weight and her colour was improving. There was still a slight "lead line" round the gum margins. Blood count figures at this time were:

        Red blood cells 3,070,000
        Haemoglobin 63 per cent
        Colour index 1.03
        White blood cells 6,400

        Reticulocytes 7.25 per cent.

Blood films presented a fairly normal appearance, stippled erythrocytes being seen only very occasionally in the Leishman stained blood film.
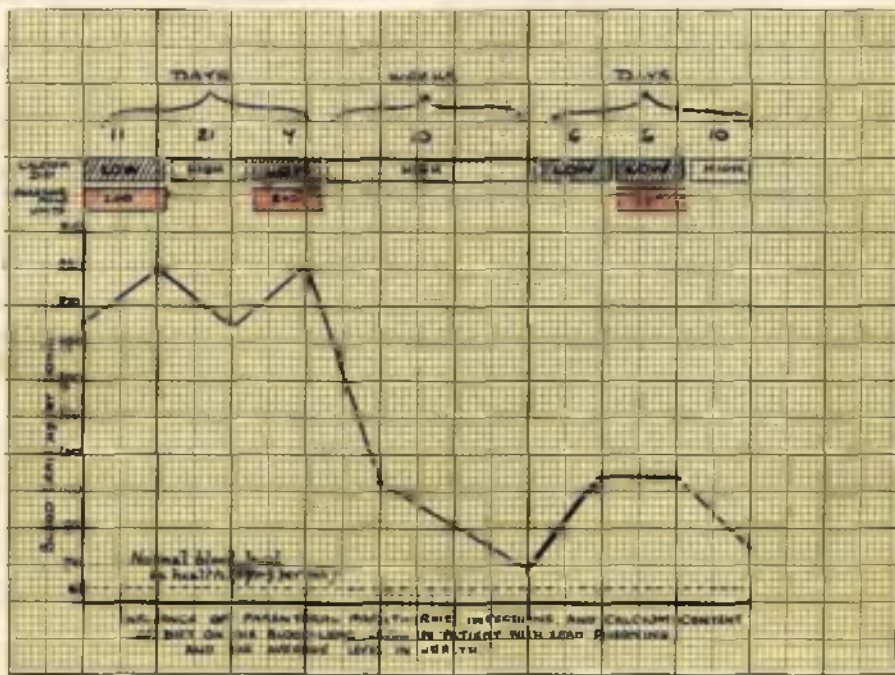
CHART 11.

She was dismissed from hospital ten weeks after admission, with instructions to continue on a high calcium diet. She was still having iron orally and liver extract injections weekly.

Two months later she was readmitted to hospital for further investigation and was placed on a low calcium diet. A further course of 240 units of parathormone was given. On this occasion there was no increase in the blood lead value following the injections. It was of interest to note that the blood lead level rose from 65 μg. when on a high calcium intake to 120 μg. per 100 ml. when on a low calcium intake. After returning to a high calcium diet following the course of para-thormone the blood lead level again fell to 75 μg. per 100 ml. By this time blood count figures were:

```
Red blood cells   3,880,000
Haemoglobin   77 per cent
Colour index 1.0
White blood cells 6,100
```

Reticulocytes 2.5 per cent

No stippled cells could be demonstrated after repeated examinations of blood films stained by Leishman's method, the erythrocytes appearing normal in shape and size.

Clinical examination of the patient was satisfactory. The "lead line" had disappeared. Blood pressure was 125/95 mm. Hg. By the ordinary tests the urine had been normal throughout. Her colour had greatly improved and menstruation had now returned. She stated that she felt in normal health.

Further observation of this case was rendered impossible as the patient went to live in the South of England. She has written on several occasions however, stating that she is in excellent health.

Remarks on the case:

The toxic effects of a salt so soluble as lead acetate soon showed themselves. After three days of "treatment" - when 12 grains had been taken - she felt sick and had suffered from abdominal pain. Ockerblad (1923) recorded severe poisoning resulting from the erroneous ingestion of 20 grains of lead acetate over a period of two weeks.

The woman's determination in continuing to take lead in spite of it practically killing her is remarkable. She stated that she had obtained the "medicine" from a man who had apparently been making a regular business of selling it. As her husband was a soldier and was going abroad, together with the fact that it took her all her time to keep herself and one child on the money she had, she felt compelled to use measures to avoid having another child. A Procurator Fiscal's enquiry led to the detention of the person selling the abortifacient. As no medical man could definitely prove that she had had a recent pregnancy, the case against the patient was dropped.

Her symptoms on admission to hospital were very severe. High calcium intake quickly relieved the colic. Subsequent de-leading with low calcium intake and parathormone caused a slight rise in the blood lead level and a marked increase in the serum calcium. This was sufficient to cause a return of symptoms which, however, quickly responded to treatment with intravenous calcium gluconate. Clinical improvement was maintained on a high calcium intake. A return to low calcium diet three months later caused the blood lead value to rise, but on this occasion parathormone did not influence the content of lead

in the circulating blood.   As suggested by Hunter and Aub (1927)
a type of "immunity" to the hormone is obtained after the first
course of injections.

There was a very high stippled cell count, the anaemia
appeared macrocytic and the colour index was over unity.   It slowly
responded to treatment with parenteral liver and oral iron.

Although this patient was very severely poisoned, no
apparent organic damage occurred in the nervous system.   The renal
tract also seemed to have been unaffected.

The legal aspect of this case is rather interesting.
In Scotland criminal abortion is a crime at common law (Glaister,
1938), and as she could not be proved to have been pregnant the
case against her was dropped.   If the case had occurred in England
it would have come under the Offences against the Person Act, 1861,
which states that a woman is guilty of felony if she takes a drug
to procure abortion whether she be or be not with child.

Numerous instances in which lead has been taken as an
abortifacient - together with opinions expressed by learned judges -
are given by Parry (1932), and he points out that it was not until
1917, 17 years after Ransome (1900) wrote of the clamant need for
this action, that diachylon was put on Part I of the Poison Schedule.
Nowadays, as already stated, the sale of all lead preparations is
further restricted.

DISCUSSION.

Although most of the results arising from the work
described in this thesis have been discussed in their appropriate
sections, there remain several points still to be considered.
The most important of these is the question of what criteria have
to be regarded as evidence of undue absorption of lead and what
findings constitute a diagnosis of lead poisoning.

With regard to absorption, the most delicate test is that
which determines the amount of lead in the systemic blood.   Hunter
(1936) stated that the only proof of lead absorption was to find lead
in the urine.   The author regards the determination of the blood lead
value as a much more sensitive method of proof of this occurrence.
As has been shown, it does not run parallel to urinary excretion of
lead and, as the de-leading experiments demonstrated, faecal
excretion is more important than that in the urine.

It has been shown that diet and metabolic upsets cause rapid
and marked changes in the content of lead in the blood and therefore
too great significance should not be attached to any single result.
Repeating the test after a 'provocative acidosis' might prove of
value in this respect.

Although anaemia and stippling of the red cells are widely
regarded as evidence of increased absorption, stippled cells may be
found in persons with little or no anaemia and a man may have a raised
blood lead value with only slight anaemia and no stippling of the

erythrocytes.   As a rule, however, stippling is associated with
a reduction in both haemoglobin and red cells, and the blood lead
value in such cases is usually over 150 μg. per 100 ml.   There is
often a reticulocytosis of over 5 per cent on examination of intra-
vitally stained blood films from such cases.   These findings
constitute definite proof of increased lead absorption.

Working conditions in industry should be such that lead
absorption is reduced to a minimum.   In general, one can assume
that the following constitute evidence of excessive lead absorption
which in time would probably lead to ill-effects:

(1)   A reduction in haemoglobin below
80 per cent (Sahli).

(2)   An increase in stippled cells over 1,000
(Leishman) or 3,000 (alkaline methylene blue) per million
red cells.

(3)   A blood lead value over 150 μg. per 100 ml.

As well as medical inspection, regular testing of lead
workers on the above lines should, in the author's opinion, be made
necessary by law.   By this means susceptible individuals could be
transferred to less hazardous occupations and the incidence of plumbism
and its numerous 'masked symptoms' be further reduced.

As to what constitutes a diagnosis of lead poisoning
opinions differ, and it is a matter of extreme importance involving
as it does, compensation of the workman.   Each case has to be
considered on its own merits, carefully assessing evidence derived

from the history, clinical examination and special investigations. As has been shown in this thesis, the presence of stippling of the erythrocytes and a raised blood lead value does not constitute a diagnosis of lead poisoning. The same applies to other analyses.

On reviewing the literature it appears that there is some confusion with regard to the modern treatment of plumbism with calcium and the employment of de-leading measures. Hunter urges the greater need of appreciation between agents which store lead in the body and those which assist its excretion. The acidosis method of treatment is so potent that its use during colic or any other toxic episode may prove fatal, due to further mobilisation of lead at a time when the reverse procedure is essential. Many text books do not stress the point sufficiently and indeed, there are some very bad mistakes — such an authority as Ling (1937) misquoting Aub as stating that "immediate alleviation of lead colic is to be expected after the intravenous injection of ammonium chloride"! Currie (1938) writes that lead is caused to remain in the bones by giving a high calcium diet and parathyroid extract. The author has personal experience of reputable physicians prescribing drugs to cause lead mobilisation during the toxic episodes of plumbism. Considering the uniformly successful and frequently dramatic results obtained by appropriate treatment, it is regrettable that its proper value is not more widely appreciated.

Lead poisoning is bound to occur as long as lead is
mined and manufactured. Although less poisonous substances have
to some extent been substituted for lead in certain trades (e.g.
paint and glaze manufacture) there are many (e.g. accumulator works)
where its use is essential or where it is either impracticable
and/or unprofitable to use other materials.

Prevention of industrial lead poisoning is the concern
of officials of the Home Office, medical officers, employers and
employees co-operating so that working conditions may be rendered
as safe as possible. Much has been done, but the task is
unfinished and high standards must be maintained. Many cases of
lead poisoning come from small concerns, where although there is
examination by Factory surgeons this is at times a mere ritual of
inspection and subsequent signing of the register. A more careful
examination, together with testing of the blood would cause plumbism
to be even less common and also reduce the somewhat innominate cases
where there is increased lead absorption and obscure, ill-defined
symptoms.

Lead workers are well paid, but they should not spend
their earnings on alcohol - which has been seen quite frequently by
the author. One potential fatal poison in the body is enough.
They should be picked men, of good character and they themselves should
realise the possible dangers of their calling. A careless man,
if poisoned, has himself to blame and does not deserve compensation,
although naturally, he gets it.

Non-industrial plumbism is practically always due to
carelessness or lack of thought on the part of someone.   Women
who take lead as an abortifacient usually do so in ignorance of its
general effect.   Cases of acute and chronic lead poisoning are
occasionally met with in those who have had lead treatment for cancer;
such therapy is to be deprecated, and has now fallen into disuse
for the most part, although a few still adhere to it.

———————————

(8)   Hospital patients with known previous exposure to lead, yet
not suffering from plumbism in the accepted sense were, in
5 per cent of cases, found to have blood lead values over
0·g. per 100 ml.   It is tentatively suggested that lead
may have been connected with certain diseases.   Although the
does not consider it likely that lead does give rise to
ptic ulceration four out of five lead workers to hospital
account with some condition had raised blood lead levels,
e of them being as high as per 100 ml.   It is
ssible that the therapeutic insuration of lead was not
...

RESULTS AND CONCLUSIONS.

(1)   Lead is a normal constituent of human blood. Persons with
        no occupational exposure to lead have blood lead values
        ranging from 30 to 89 μg. Pb per 100 ml., this being derived
        from the diet and atmospheric dust.

(2)   Apparently healthy lead workers have blood lead values
        ranging from 52 to 192 μg. Pb per 100 ml.   There is no
        apparent correlation between age, length of exposure to lead
        and blood lead value.   Men with severe exposure to lead have
        sometimes appreciably high blood lead values, but this is
        not always the case.

(3)   Hospital patients with known previous exposure to lead, yet
        not suffering from plumbism in the accepted sense were, in
        25 per cent of cases, found to have blood lead values over
        100 μg. per 100 ml.   It is tentatively suggested that lead
        may have been connected with their illnesses.   Although the
        author does not consider it likely that lead can give rise to
        peptic ulceration four out of five lead workers in hospital
        on account of this condition had raised blood lead values,
        one of them being as high as 187 μg. Pb per 100 ml.   It is
        possible that the therapeutic administration of alkalies had
        caused this. by mobilising lead from the bones.

(4)   The blood lead value in clinical plumbism may range from 109
        to 380 g. Pb per 100 ml.   The figure depends to a great extent

on the nature of the diet.   With high calcium intake it may

fall to within normal limits in a few days.   With de-leading

it may rise to 1,000 μg. per 100 ml. or more, equally rapidly.

(5)   There is no 'threshold' of blood lead value at which symptoms

of plumbism appear.   Values over 100 μg. per 100 ml. indicate

that increased absorption of lead is taking place, or has

occurred in the past.   There is no close correlation between

blood lead value and the amount of lead in the excreta.

(6)   Analysis of biological materials for lead by the dithizone

method is relatively rapid, involves little apparatus, and is

accurate.

(7)   Stippling of the red cells (punctate basophilia) in stained

blood films does not necessarily indicate lead poisoning.   It

was found in 77 per cent of 44 apparently healthy lead workers.

This change of the red cells can be noted in men with little

anaemia, although larger numbers of them can as a rule be found

in those with lowered haemoglobin values.   The average

haemoglobin values of the above lead workers ranged from 75

to 100 per cent, with a mean of 91 per cent (Sahli).

(8)   Stippling can be more easily demonstrated by staining with

alkaline methylene blue than by Leishman's method.   Using

the former technique very occasional finely stippled cells

were found in nearly 8 per cent of a series of 115 healthy

individuals with no known industrial lead risk.   It is just

possible that the occasional presence of such cells may be due

to the 'normal' amount of lead in the blood, but they are
more probably certain young red cells showing this alteration
due to staining by an alkaline single dye solution.

(9)   It would seem that stippling is an alteration of the poly-
chromatic substance in the cytoplasm of young red cells. ·
Stippled and polychromatic cells of the methylene blue or
Leishman stained films are probably identical with the reticulo-
cytes of intravitally stained films.

(10)   Although the morbidity of industrial lead poisoning has been
enormously reduced, cases will continue to occur as long as
it is manufactured and used.   There is no practicable substitute
for lead in very many industries.   With modern conditions
in industry, which are still improving, the incidence of the
disease should fall still further.

(11)   Laboratory methods should be further employed in assessing
the degree of exposure of lead workers.   Regular performance
of haemoglobin estimations, stippled cell counts and, if possible,
estimations of blood lead values would enable persons showing
evidence of increased lead absorption to be moved to less
hazardous work.   Such tests should be performed every three
or four weeks.

(12)   The most sensitive test for increased absorption of lead is
estimation of the lead content of the blood. Values over 150μ g.
per 100 ml. should be regarded as unduly high.   A total
excretion of over 0.6 mg. Pb per day is also excessive.

(13) A stippled cell count of over 5,000 per million red cells
      in a blood film stained by alkaline methylene blue is also
      indicative of/increased lead absorption, as is a reticulocyte
                unduly
      count of more than 3 per cent or a haemoglobin value of under
      80 per cent - although these latter tests are much less
      specific.

(14) A 'lead line' in the gums does not necessarily indicate
      plumbism, although it always indicates excessive lead
      absorption.

(15) The diagnosis of lead poisoning is essentially clinical, although
      laboratory tests may provide valuable additional information.

(16) Anaemia and colic are now the commonest manifestations of
      clinical plumbism.   Paralysis and encephalopathy are rare.

(17) Certain cases described in the text were diagnosed as
      "increased lead absorption" rather than plumbism when there
      was only laboratory evidence of increased lead exposure to
      account for their obscure symptoms.   In such cases none of
      the typical clinical symptoms of lead poisoning in the
      generally accepted sense were present, and although standards
      of diagnosis vary the author contends that only cases showing
      <u>clinical</u> evidence of the disease should be regarded as
      "plumbism".

(18) A man should never return to work in a lead trade if he has
      once suffered from plumbism or shown definite evidence of
      increased absorption associated with the less typical ill-effects.

(19)   Treatment with a high calcium intake (oral and parenteral)
       is of outstanding value during the toxic episodes of
       plumbism, and is also of value in lowering the blood lead
       values of those with "increased lead absorption", and in
       causing general improvement.   It is of no value in lead
       encephalopathy.

(20)   De-leading of cases of plumbism should not be carried out
       without careful control and consideration of other factors,
       such as renal function.   Ammonium chloride and a low calcium
       diet have proved to be a satisfactory method of this treatment.
       It is cheaper and apparently a more effective method than
       parathormone injections associated with a low calcium diet.

(21)   Preventive treatment is of primary importance in both
       industrial and non-industrial plumbism.   Legal standards even today
       are frequently not regularly adopted in factories, and more
       stringent enforcement of regulations is required.   Standards
       close to perfection can be attained, and a more widespread
       appreciation of this is desirable.

(22)   Symptomatic treatment with calcium frequently causes great
       improvement, and enables a man to return to an employment where
       there is no lead hazard.   He can again become a wage-earner
       and enjoy good health, although he probably never rids himself
       of the excess lead in his body.   As long as his diet and habits
       of life remain satisfactory the lead remains in the bones,
       where it is innocuous.

SUMMARY.

(1)   The history, biochemistry and physiology of lead are discussed, and blood lead values of normal healthy individuals with no lead hazard, healthy lead workers, hospital patients not suffering from plumbism with known lead contact, and cases of clinical plumbism are recorded and contrasted.

(2)   The aetiology, pathology, clinical findings and treatment of plumbism are discussed.

(3)   Seven cases of clinical plumbism of industrial origin are described.   Three individuals showing laboratory evidence of increased lead absorption of industrial origin, associated with ill-defined symptoms, are also recorded.

(4)   Lead poisoning arising from the drinking of lead-contaminated water, resulting in the death of a woman, is described, together with investigations carried out to detect the cause of the poisoning.

(5)   A case of severe plumbism following the ingestion of 110 gr. lead acetate for the purpose of criminal abortion is recorded and discussed.

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