Lead

Atomic number 82
Atomic weight 207.19

Collection

Blood	2mL	Plastic container with EDTA anticoagulant
Urine	20 mL	Sterile Universal

Reference ranges

			Reference
Serum/plasma			
Blood	µmol/L	Less than 0.23	1, 2
Urine	nmol/L		
	nmol/L	13.6	6
	nmol/24 h	1.3-39.4	
	nmol/mmol creatinine	0.11-3.3	
	µmol/mol creatinine	Male 8.8 (95th percentile) Female 1.26 (95th percentile)	7

Notes

Occupational exposure monitoring [3]

Category	Blood Lead (µg/dL)*	Maximum interval between blood lead measurements
A	under 30	12 months
B	> 30 < 40	6 months
C	> 40 < 50	3 months
D	> 50 < 60	3 months
E	60 and over	at the doctor's discretion but not more than 3 months

Women of reproductive capacity and young persons whose exposure to lead is significant should have their blood lead concentrations measured at intervals of at least every three months.
* 1 µmol/L = 27 µg/dL

References

1. Advisory Committee on Childhood Lead Poisoning Prevention. Low level lead exposure harms children: a renewed call for primary prevention. Atlanta, GA: US Department of Health and Human Services, CDC, Advisory Committee on Childhood Lead Poisoning Prevention; 2012. Available at http://www.cdc.gov/nceh/lead/acclpp/final_document_010412. pdf. Accessed May 18, 2012.
2. CDC. CDC response to Advisory Committee on Childhood Lead Poisoning Prevention recommendations in “Low level lead exposure harms children: a renewed call for primary prevention.” Atlanta, GA: US Department of Health and Human Services, CDC; 2012. Available at http://www.cdc.gov/nceh/lead/acclpp/cdc_response_lead_exposure_recs. pdf. Accessed May 18, 2012.

3. Control of Lead at Work Regulations. HSE 2002
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5. Sieniawska C, Jung L, Olufadi R, Walker V. Twenty four hour urinary trace element excretion: reference intervals and interpretive issues. Ann. Clin. Biochem. 2012; 49: 341-351
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Clinical

Lead is a non-essential element. Toxic effects resulting from its extensive use in silver smelting, paint production, jewellery making, ceramic glazes, building construction, and in drinking vessels and water supply systems have been known for many hundreds of years. During the last 150 years the industrial use of lead has increased enormously and since the mid-1920s the use of alkyl lead derivatives as anti-knock agents in petrol has caused a further massive increase.

Toxicity

Through the introduction of stringent safety precautions in industry, and regulations limiting the amount of lead in paints, the number of cases of severe inorganic lead poisoning has fallen dramatically. Isolated instances of toxicity, both industrial and non-occupational, do however occur, with symptoms of abdominal pain, fatigue, weakness, anaemia, basophilic stippling of erythrocytes, and peripheral neuropathy. Rarely, a blue line in the gums is seen and chronic renal failure may occur. Radiological examination may reveal radiopaque material in the abdomen and bands of increased density ('lead lines') in the bones. In children, severe effects are more common and may lead to encephalopathy and death.

The use of tetramethyl and tetraethyl lead in the petroleum industry has greatly reduced since they were removed as additives in petrol in the UK. The incidences of cases of direct toxicity from absorption of these compounds are also relatively rare. The pathological picture differs considerably from inorganic lead toxicity in that neurological signs such as encephalopathy, delirium, confusion, anorexia, vomiting, weakness and fatigue predominate. Cases may arise however from activities such as petrol sniffing by young people, although the situation is complicated by the toxic effects of the petroleum hydrocarbon.

Although cases of severe lead toxicity still occur, increasing anxiety has been expressed in recent years over the possible effects of prolonged sub-clinical lead exposure on neurobehavioural development. A number of studies have shown associations between blood lead concentrations of less than 0.48 µmol/L and intellectual development in children and cardiovascular disease in adults and children. A summary of recent research on low blood lead concentrations in children has been compiled by the Global Lead Advice and Support Service.

In certain areas of the country, the combination of soft water and extensive use of lead plumbing and storage tanks has caused particular concern; slightly acidic water may also leach lead from badly soldered copper supply pipes. Pica, the repetitive ingestion of non-food substances by young children, may present a hazard in poorly maintained housing with lead-based paint.

Measures such as the removal of tin-lead solder from food cans and the control of lead levels in paints have helped over the last 15 - 20 years to reduce environmental exposure to lead. There seems little doubt, however, from the results of studies comparing subjects in light and heavy traffic areas of the UK, that the increasing use of lead free petrol has resulted in a very significant fall in the blood lead levels in populations exposed to traffic emissions. Results from the most recent population survey of blood lead concentrations in the United States showed that the 97.5th percentile is at 5 µg/dL (0.024 µmol/L) and this is now the CDC upper reference value, replacing the previous 10 µg/dL ‘level of concern’.

The traditional remedies of a number of ethnic groups may contain substantial amounts of lead and several instances of clinical lead poisoning by ingestion of Asian traditional remedies have been reported in the U.K. Middle Eastern and Asian eye cosmetics may also contain lead, and their use on infants or by their mothers is associated with increased blood lead levels in the infants concerned.

An examination of cases in the UK where children have been found to have blood lead concentrations greater than 0.48 µmol/L showed that the principle sources of exposure were pica (ingestion of leaded paint), use of ethnic remedies and dust from old paint produced during redecorating.

Multiple layers of paintwork chewed by an infant who developed severe lead poisoning.

Laboratory Investigations

Blood lead assay is the measurement of choice for the assessment of exposure to inorganic lead as 95% of the blood lead is bound to erythrocytes. For assessment of exposure to organic lead derivatives however, urinary lead estimation is the determination of choice. Absorbed organic lead penetrates into the lipophilic tissues of the body and only a very modest rise in blood lead concentration may be observed.

Lead is known to affect a number of important enzyme systems in the body including those involved in haem synthesis. Importantly, δ-ALA dehydratase and ferrochelatase are inhibited by lead. Measurement of δ-ALA dehydratase is a particularly sensitive indicator of lead exposure although this extreme sensitivity renders the test of little value in routine clinical practice. The reliability of blood lead measurements has rendered use of urinary determinations such as δ-ALA and coproporphyrin largely obsolete. Although, their use for industrial monitoring is still promulgated by various statutory requirements (see below) they are rarely used in modern practice.

A convenient supplementary assay is that of zinc protoporphyrin (ZPP) in blood, the concentration of which is increased in lead exposure. This can be carried out on capillary blood samples using a purpose designed fluorimeter. Although its correlation with blood lead is good where there is significant exposure, and the assay has been recommended in the United States for occupational surveys, it must be appreciated that ZPP increases in iron deficiency anaemia and that false negatives can occur in cases of acute lead exposure. It is clear therefore that the test is no substitute for blood lead determination and its usefulness, even as an initial screen, is limited.

References

1. CDC. CDC response to Advisory Committee on Childhood Lead Poisoning Prevention recommendations in “Low level lead exposure harms children: a renewed call for primary prevention.” Atlanta, GA: US Department of Health and Human Services, CDC; 2012. http://www.cdc.gov/nceh/lead/acclpp/cdc_response_lead_exposure_recs. pdf..
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3. GLASS (Global Lead Advice and Support Service). http://www.lead.org.au/fs/fst67.html
4. Menke A, Muntner PV, Silbergeld EK, Guallar E. Blood lead below 0.48 µmol/L (10 µg/dL) and mortality among US adults. Circulation 2006; 114: 1388-1394

Annex: Occupational Exposure to Lead

Certain statutory requirements exist for the monitoring of industrial workers at risk from lead exposure. An Abstract of the "Control of Lead at Work Regulations" HSE 2002 and Approved Code of Practice, is given below.

Inorganic Lead Exposure

Suitable facilities

Where medical surveillance procedures, e.g. medical examinations and blood or urine sampling, are carried out at the employer's premises, suitable facilities should be made available. These should comprise a room which is:

1. properly cleaned, adequately warmed and well ventilated
2. suitably furnished with a table and seats
3. provided with a wash-basin equipped with hot and cold running water, soap and a clean towel. If it is not reasonably practicable to provide hot and cold running water, then a supply of warm water should be provided.

The room should be set aside for the exclusive purpose of medical surveillance whenever it is required, and provision should be made for privacy. Where the number of employees to be examined or assessed is substantial, then where reasonably practicable, a suitable waiting area should be provided. An adjacent or nearby toilet with hand washing facilities should be available for employees.

Initial Medical Assessment - previously exposed employees.

An initial medical assessment should always be carried out on all new employees who have been exposed to lead at work in a previous job in the last three months, irrespective of whether their exposure to lead in their new employment is likely to be significant. Where the employee's blood or urine show the following lead concentrations, the employee concerned should be regarded as significantly exposed to lead, and be placed under medical surveillance irrespective of whether the employer's assessment concludes that they are likely to be significantly exposed to lead in their new employment.

Blood lead concentrations

(a) women of reproductive capacity - 20 µg/dL or greater

(b) all other employees - 35 µg/dL or greater

Urinary lead concentrations

(a) women of reproductive capacity - 25 µg Pb/g creatinine or greater

(b) all other employees - 40 µg Pb/g creatinine or greater.

The subsequent monitoring of the employee's blood/urine concentrations should be carried in accordance with the guidance given below.

Lead and Lead compounds, except lead alkyls

Initial medical assessment

The employer should notify the doctor of the name of each person newly employed or whom it is intended to employ on work which is likely to expose that person significantly to lead so that the doctor can carry out the initial medical assessment.

The initial medical assessment should be carried out before or within 14 days of a person starting work for the first time which is likely to result in significant exposure to lead. The assessment should consist of:

1. consideration of the employee's occupational record with particular reference to any earlier exposures to lead, and any previous suspensions;
2. a clinical assessment including consideration of medical history, clinical conditions, and personal hygiene and intellectual capacity to work with hazardous substances;
3. measurement of 'baseline' blood-lead and haemoglobin.

The doctor may also want to verify the results of initial baseline measurements by carrying out some of the further biological tests mentioned below.

Periodic medical assessments

These should be carried out and consist of:

1. measurement of blood lead concentrations;
2. other relevant biological tests where indicated;
3. at least once a year a clinical assessment; and
4. at least once a year may also include a measurement of haemoglobin and ZPP concentrations.

For employees other than women of reproductive capacity and young persons, the frequency of carrying out periodic medical assessments may be determined by the doctor so long as the employee's blood lead concentration remains below the appropriate suspension level.

Monitoring an employee's blood lead concentration.

When employees are significantly exposed to inorganic lead compounds, their blood lead levels should be measured every three months. If exposure is uniform, then a consistent blood lead pattern will probably be established, although this may take about a year. Thereafter, except for women of reproductive capacity and young persons, blood lead measurements can be taken at the reduced intervals shown in the table below.

Category	Blood Lead (µg/dL)	Maximum interval between blood lead measurements
A	under 30	12 months (see note below)
B	> 30 < 40	6 months
C	> 40 < 50	3 months
D	> 50 < 60	3 months
E	60 and over	at the doctor's discretion but not more than 3 months

Category A indicates that the absorption of lead due to occupational exposure is reasonably well controlled. The interval between blood lead measurements should not however be longer than 6 months unless on the previous two consecutive occasions on which air monitoring was carried out, measurement of the airborne lead to which that person was exposed was less than 0.075 mg/m^3.

Category B indicates that lead is being absorbed due to occupational exposure to lead. For employees in this category other suitable biological tests may be carried out in addition to 6 monthly blood lead measurement. Suitable biological tests include measurement of zinc protoporphyrin (ZPP), erythrocyte protoporphyrins, aminolaevulinic acid dehydratase in blood (ALAD) and aminolaevulinic acid in urine (ALAU) and may be carried out every 12 months.

Category C also indicates that lead is being absorbed due to occupational exposure but at a higher concentration than for employees in Category B, and that blood lead concentrations may be approaching the action level. Other suitable biological tests may also be appropriate as for Category B employees.

Category D the blood lead concentrations have breached the action level and the employer should initiate an investigation in accordance with the procedure given below. This range of blood lead concentrations also represent the level at which the employee should come under direct medical surveillance in that a clinical assessment and any other relevant biological tests should be carried out as soon as possible after the blood lead concentration has been confirmed. The clinical examination may be deferred until measurement of the blood lead concentration carried out at a time determined by the doctor shows that the action level of 50 µg/dL continues to be breached.

Category E represents the concentration above which the doctor may certify the employee as unfit for work where there is liable to be exposure to lead.

Some exposures, like the burning of lead paint, covered metal during demolition work, scrap metal work etc. are however likely to be so variable that a clear pattern of lead absorption cannot be established. In these cases, it may be necessary to continue three-monthly blood lead tests for as long as medical surveillance is required, or even more frequently if the doctor thinks this necessary.

Women of reproductive capacity and young persons whose exposure to lead is significant should have their blood lead concentrations measured at intervals of at least every three months.

Action level

All employees who are likely to be exposed to lead at work, other than lead alkyls, should be made subject to a blood lead concentration action level. The purpose of the action level is to prompt the employer to investigate why

it has been breached and to review the range and effectiveness of control measures used with the aim of reducing the employee's blood lead and of preventing it from reaching the suspension limit. In investigating why the action level has been breached, the employer's review should include the following:

1. a check that recommended and established work practices are being followed;
2. a check on the effectiveness of all control measures, including where appropriate that engineering controls are working as they should to their design specification and do not need repair
3. where appropriate, any respiratory protective equipment is being properly used in accordance with instruction; and
4. the employee(s) is following strict hygiene procedures; and
5. consultation with the doctor to agree any additional protective or preventive measures to be taken for any selected individuals or groups of employees.

Suspension limit

All employees who are liable to be exposed to lead at work are subject to a suspension limit. This is the blood lead concentration at which the doctor decides whether to certify the employee as unfit to go on working with lead in order to protect the employee from developing the symptoms of blood lead poisoning.

Any employee whose blood lead concentration reaches the appropriate suspension limit should have the test repeated urgently. If the result of the repeat test is also equal to or greater than the appropriate suspension limit, the doctor should certify the employee as unfit for work which exposes the employee to lead. However, some employees, excluding women of reproductive capacity and young persons, who have worked a long time in the lead industry, may have built up a high body burden of lead which could take a long time to fall below their suspension limit of 60 µg/dL For these employees only, the doctor may use discretion in deciding whether to recommend suspending them from further work with lead. The doctor need not recommend suspension if the employee's blood lead concentration is not more than 70 µg/dL and the ZPP level remains lower than 20 µg/g haemoglobin or the ALAD level remains greater than 5 European units or the ALAU level remains lower than 20 mg/g creatinine.
When taking advantage of this discretionary clause, the doctor should consider increasing the frequency of blood lead and haemoglobin testing. For employees with blood lead concentrations greater than 60 µg/dL but not more than 70 µg/dL who are not suspended from work, the employer should nevertheless make every effort to reduce the employee's blood lead concentration to below 60 µg/dL.

The doctor may also use discretion to certify an employee as unfit for work which further exposes that employee to lead where the employee's blood lead concentration is below the suspension limit; eg where the results of other biological tests or a clinical assessment suggests such action pending further investigation; or there is evidence that the employee is suffering from one of the conditions referred to previously.

Women of reproductive capacity

If the blood lead concentration of a woman of reproductive capacity triggers the suspension level but the doctor does not certify her as unfit to continue in work which exposes her to lead, the doctor should record the reasons in the employee's health record e.g. the woman has left the employment concerned.

To safeguard any developing foetus, if a woman of reproductive capacity who is employed on work which exposes her to lead becomes pregnant, she should notify her employer as soon as possible in accordance with the requirements of the Management of Health and Safety at Work Regulations 1992. The employer should in turn notify the doctor and suspend the pregnant employee from any work involving exposure to lead.

Lead alkyls

The method for monitoring the uptake of lead alkyls in the body is by measuring total urinary lead concentration, and the concentration of analytes in urine is corrected for the urinary creatinine concentration to allow for differences in the volume of urine produced. The urine analyte concentration is then corrected to what it would be if there were 1 gram per litre of creatinine in the urine, and values are then expressed in units of µg Pb/g creatinine. This biological monitoring method should be used for carrying out initial and periodic medical assessments on employees exposed to these particular lead compounds.

The general arrangements described above for carrying out initial and periodic medical assessments also apply to employees who are exposed to or who work with lead alkyls. However, at least once a year the medical assessment should consist of the measurement of blood lead as well as of urinary lead concentrations and, where the results of these indicate the need for it, a clinical assessment.

The intervals between carrying out periodic urinary lead measurements should be determined as set out in the table below.

Group of Employees	Urinary lead as µg Pb/g creatinine	Maximum interval between urinary lead measurements
All employees except women of reproductive capacity and young persons	under 95 95* - 109 110 and over **	6 weeks 1 week doctors discretion
Women of reproductive capacity	under 20 20* - 24 25 and over**	6 weeks 1 week doctors discretion

Note * represents the level at which the employee will come under closer medical surveillance.