Trace metals Information for Test Manager

Biological handbook 2012 and Clinical Methods Doc

Aluminium in Plasma

Introduction

Glossary

Dialysis dementia
A fatal neurological syndrome in patients with chronic renal failure on long term intermittent haemodialysis treatment.

Dialysis osteodystrophy
A progressive metabolic bone disease characterised by crippling bone pain and fractures.

Iatrogenic
An adverse reaction in a patient that has occurred as a result of treatment.

Aluminium is the most abundant metal in the earth's crust, 8.8% by weight, exceeded in abundance only by oxygen and silicon. Aluminium does not occur naturally in the metallic state; however it is widely distributed in rocks, clay and soils in the form of gems such as ruby, sapphire and turquoise and in minerals of industrial importance such as alum, bauxite, cryolite, corundum and kaolin.

Because of the ubiquitous distribution of aluminium compounds, natural human exposure is unavoidable, and moderate amounts of the element enter the body constantly through inhalation of atmospheric dusts and ingestion of food and drink. Despite an oral intake ranging from 5-10 mg daily, little aluminium is absorbed and serum levels of 0.07-0.30 μmol/L are usually found. Tissue aluminium levels are very low. No biological function for the metal has been found, moreover, life has evolved in an environment so rich in aluminium that it would be surprising if human beings could not tolerate substantial variations in exposure without ill effects. Under most circumstances this tolerance appears to hold. Industrial aluminium toxicity is rare and tissue concentrations of the metal have apparently been affected little by extensive use of aluminium products and cookware. The application of thousands of kilograms of aluminium products as antiperspirants has not caused toxicity except for occasional local irritation. Indeed, a considerable body of experimental data gathered over many years suggests the presence of formidable epithelial barriers to aluminium absorption in the lung, the gastrointestinal tract and the skin.

High levels of aluminium can accumulate in the tissues of patients with chronic renal failure[2] on long term haemodialysis treatment. The increased tissue load of aluminium may be derived from:

1. Intestinal absorption following administration of aluminium hydroxide gels used to control the high plasma phosphate levels found in chronic renal failure (May also be used as an antacid). Patients have in the past ingested up to several kilograms of elemental aluminium over their dialysis 'career'

2. Water used for haemodialysis may contain aluminium which will dialyse across the dialysis membrane and lead to raised plasma aluminium and tissue

aluminium levels. A single dialysis may expose the patient's blood to as much as 250 L of water (39 000 L per year)

3. The dialysis concentrate used to prepare the dialysate may contain high levels of aluminium and lead to substantial contamination of the dialysate fluid

The increased tissue content of aluminium appears to be the major factor in the aetiology of dialysis dementia and dialysis osteodystrophy. The prevention of iatrogenic aluminium poisoning involves caution in the use of aluminium containing oral phosphate binders, together with regular monitoring of:

i. the aluminium content of the dialysate
ii. the domestic tap water used to prepare the dialysate and
iii. monitoring of serum aluminium levels in patients on long term haemodialysis treatment

Specimen Requirements

6 mL K2 EDTA (Royal Blue) whole blood.
The plasma should be separated from the red cells within 4 hours, aliquot 1 mL plasma, refrigerated 4°C.

Aluminium in Urine

Introduction

Aluminium is used in a wide range of industrial processes such as the manufacture of alloys, window frames, engine parts, aircraft parts, roofs, electric wires etc.

Aluminium is mainly absorbed through the lungs by inhalation of fumes and fine dust particles. Some aluminium is absorbed through the gastrointestinal tract when large amounts of high aluminium containing compounds are ingested, such as antacids. It is largely excreted via the urine, although some is also excreted in the bile.

Measurement of urine aluminium is used to monitor workers occupationally exposed to fumes and dust. Welders have the highest excretion levels among exposed workers.

The half life of aluminium is 8 hours, a relatively short period, at first exposure. However, this increases with the length of exposure, and can reach 6 months after 10 years of exposure.

Sample requirements

Aluminium is widespread throughout the environment, so care must be taken when collecting the sample.

6 mL random urine. Post shift – The last two hours to immediately following the end of the working day. Ensure that hands are washed and clothes are free of contamination.

Interpretation

Occupational exposure to aluminium fumes and dust has been associated with pulmonary fibrosis

Antimony in Urine

Introduction

Antimony is a brittle silver-white metalloid obtained from the sulphide ore stibnite. It is mainly used as a fire retardant for paint, plastics, textiles, paper, rubber and adhesives and in the glass production industry. Its use as an alloy with lead in storage batteries has greatly decreased. It is also used in the semiconductor industry.
It is frequently found together with arsenic and some of the toxic effects described in the past may have been due to arsenic. Organic antimony compounds are used in the treatment of Leishmaniasis which can lead to toxicity.
Antimony is ingested or inhaled and is rapidly excreted in the urine and faeces. Inorganic trivalent antimony compounds are conjugated with glutathione and mainly excreted in the bile and pentavalent compounds in the urine.
Stibine, antimony hydride (SbH_3) is a highly toxic colourless strongly smelling gas which is formed when an acid reacts with a metal alloy containing antimony. Exposure can happen when charging lead batteries. It is extremely toxic causing haemolytic anaemia and tubular necrosis.

Toxicity

Symptoms of exposure are similar to arsenic but much less toxic. Dermatitis and irritation of the mucous membranes used to be common along with a simple pneumoconiosis among process workers with chronic exposure, but as conditions have improved symptoms have become uncommon.
Acute exposure to Stibine gas causes headache nausea and vomiting.

Sample requirements

20 mL random urine. Post shift – The last two hours to immediately following the end of the working day. Ensure that hands are washed and clothes are free of contamination.

Interpretation

No Biological Exposure Index is available for Antimony however a level of 32 nmol/mmol (35µg/g) creatinine has been proposed for workers exposed to pentavalent Antimony compounds.[7]

Arsenic in Urine

Introduction

The main exposure to arsenic in New Zealand occurs in the timber treatment industry. The preservation of timber (tanalising) is carried out using a mixture of salts of copper sulphate, potassium dichromate and arsenic pentoxide. The timber is pressure injected with the preservation liquid in large pressure cylinders, after which it is stacked in the yard while still wet with preservation chemicals. Arsenic may also be encountered in the plating industry and in foundries and glassworks, and is found in some fruit tree sprays.

Sample requirements

6 mL random urine. Post shift – The last two hours to immediately following the end of the working day & End of Work Week – After at least 4 days of exposure. Ensure that hands are washed and clothes are free of contamination.

The testing method used measures only inorganic arsenic levels in the urine, so it is not necessary but desirable to exclude seafood (organic arsenic) from the diet prior to urine collection.

Frequency of biological monitoring

The concentration of arsenic in urine generally reflects very recent exposure. The frequency of biological monitoring is thus dependent on whether the work is seasonal. For example:

Seasonal timber treatment

Initial testing should be made in the first few weeks of timber treatment. If the results are normal and adequate precautions are being taken, the tests need not be repeated until a change occurs in work patterns or environment.

Regular timber treatment

Workers should be tested at least yearly. If the results are normal and adequate precautions are being taken, the tests need not be repeated until a change occurs in work patterns or environment.

If urine results are elevated (above the Biological Exposure Index), and it is unclear what the source of the potential exposure is, then the laboratory suggests the following protocol is followed:

Do a follow-up test at the end of a further working week, then re-test on the following Monday (after 48 hours of non-exposure coupled with avoidance of shellfish). The expectation is that the concentration would halve and may fall under the recommended limit.

Shellfish avoidance should then continue. Further testing at the end of the next working week should give a gauge of the effect of working practices and the requirement for any adjustments.

Note: The half-life of arsenic is in the order of 48 hours.
Methyl compounds (eg DMA from shellfish) can contribute to reported inorganic arsenic levels.

Barium in Urine

Introduction

Barium is an alkaline earth metal found in ores principally as sulphates and carbonates (barite and witherite respectively). The commercial use ranges from getters in electrical tubes, rodenticides, and colourants in paint and as a contrast medium in medical imaging. It is also found in oil and gas drilling muds, stabilizers for plastics, case hardening steels, bricks, tiles and lubricating oils and jet fuel. Barium occurs naturally in food and drinking water. Most exposure occurs through oral ingestion or inhalation of barium containing dust. Foods such as Brazil nuts, seaweed, fish and certain plants may contain high levels of barium. The toxicity of barium is related to the solubility and hence availability of the salt. Barium sulphate (medical contrast) being very insoluble is non-toxic as very little is absorbed. Barium carbonate which dissolves in the stomach acids is readily absorbed, as are barium hydroxide and nitrate, and these compounds are more toxic. Barium has the potential to bio-concentrate. Occupational exposure is generally in the barium mining or processing industries.

Barium exerts its toxicity through its effects on potassium channels; it is a competitive potassium channel antagonist, blocking the passive efflux of potassium from the intracellular compartment, resulting in hypokalaemia. This in turn leads to ventricular tachycardia, unstable blood pressure, muscle weakness and paralysis. Local gastrointestinal effects include abdominal cramps, vomiting and diarrhoea. Nephropathy is considered the most sensitive measure of toxicity with a clear dose response curve in animal studies.

Approximately 90% of the body burden of barium is contained in the bones and teeth; the primary route for excretion is through the faeces.

There is no data correlating exposure levels with blood or urine barium levels.

Sample requirements

6 mL random urine. Post shift – The last two hours to immediately following the end of the working day. Ensure that hands are washed and clothes are free of contamination.

Bismuth Blood and Urine

Bismuth is used in low melting point alloys and is used in malleable iron. It is added to aluminium and steel for better machinability. Bismuth compounds are used as catalysts and in semiconductors.
Bismuth compounds are used therapeutically for the treatment of gastric and duodenal ulcers. Bismuth subsalicylate appears to be effective in the suppression of Helicobactor pylori and is increasing used for the treatment of relapsing gastric ulcers.
Bismuth is rapidly excreted in the urine.

Toxicity

Severe side effects from taking bismuth compounds including gingivastomatitis, toxicity to the kidney, liver and central nervous system have been recorded. Abnormal MRI scans and encephalopathy may develop at high bismuth concentrations. This is usually reversible when treatment ceases.

Specimen requirements

6 mL K2 EDTA (Royal Blue) whole blood.

6 mL random urine. Post shift – The last two hours to immediately following the end of the working day. Ensure that hands are washed and clothes are free of contamination. Recommended sample type

Interpretation

The monitoring of bismuth levels in blood is recommended for patients undergoing oral therapy, normal levels during treatment should be below 50 ug/L(239 nmol/L), close monitoring is required at levels between 50 (329 nmol/L) and 100 ug/L (478 nmol/L) and treatment should be suspended at levels above 100 ug/L(478 nmol/L).

Bromide in Plasma & Methyl Bromide

Introduction

Methyl bromide is a gaseous chemical used as a fumigant for large enclosed industrial and agricultural areas. Bromide is also used as a sedative. Bromides act by depressing central nervous system activity and have shown moderate anticonvulsant activity against tonic seizures. They are now very seldom used as anticonvulsants.

Methyl bromide is known to be partially converted to inorganic bromide. The contribution of this metabolite to the toxicity of the parent compound is unclear, but since inorganic blood concentrations after methyl-Br poisoning are generally much lower than during intoxication of bromide salts, it seems likely that the methyl-Br is the primary toxic agent. Toxicity may develop after a latent period of several hours and is manifested by confusion, abdo pain, weakness, nausea, convulsions, coma and occasionally pulmonary edema.

Specimen

The method requires 1 mL of serum or plasma. Specimens should be collected pre-dose if therapy is being monitored.
For industrial exposure collect sample: Post shift – The last two hours to immediately following the end of the working day. Ensure that hands are washed and clothes are free of contamination.

Cadmium in Blood

Introduction

Cadmium metal is used as an anticorrosion coating for ferrous metals and in welding and brazing alloys. Cadmium compounds are used in nickel/cadmium batteries and as pigments in paints, plastics and glazes. The welding and gas cutting of cadmium coated steel carries a high risk due to the high volatility of cadmium metal. Cadmium occurs naturally with zinc and is a by-product in the smelting of zinc and some lead ores.

Cadmium has a long biological half life (10-33 years) and accumulates progressively in the body. Tobacco smoking may significantly increase exposure to cadmium, as cigarettes contain 1-2 μg of cadmium, about 10% of which is absorbed. Cadmium accumulates in the liver and kidneys, which account for 50% of the body burden, and is excreted in the urine.

Biological monitoring

- Blood cadmium reflects average intake over the previous few months.
- Urine cadmium is indicative of body burden when exposure is low to moderate.

Sample requirements

6 mL K2 EDTA (Royal Blue) whole blood.
To minimise contamination of the sample with cadmium from tobacco, the sample should be collected in a smoke free environment. Sampling time is not critical.
For occupational monitoring it is suggested that both blood and urine is collected.

Interpretation

Urine cadmium levels should be monitored for renal dysfunction in workers regularly exposed to low levels of cadmium.

Toxic Effects

Acute exposure:

Ingestion from food in cadmium plated cans or ingestion of cadmium dust affects the gastrointestinal tract and causes increased salivation, choking, vomiting, abdominal pain, diarrhoea. Cadmium ingestion can also lead to shock, renal failure and death. Inhalation of dust or fumes is responsible for most fatal industrial accidents. It causes cough, headache, vomiting and chest pain, and may lead to pulmonary edema and death.

Chronic exposure:

Renal tubule damage appears to be the main effect of chronic exposure. The time at which renal damage can occur depends on the intensity of exposure and is usually greater than 10 years. The bone damage (osteomalacia) seen in chronic cadmium exposure is secondary to renal tubule damage causing alterations in calcium, phosphate and vitamin D metabolism. Cadmium and some cadmium compounds have been listed as carcinogenic.

Cadmium in Urine

Introduction

Cadmium metal is used as an anticorrosion coating for ferrous metals and in welding and brazing alloys. Cadmium compounds are used in nickel/cadmium batteries and as pigments in paints, plastics and glazes. The welding and gas cutting of cadmium coated steel carries a high risk due its high volatility. Cadmium occurs naturally with zinc and is a by-product in the smelting of zinc and some lead ores. Cadmium has a long biological half life (10-33 years) and accumulates progressively in the body. Tobacco smoking may significantly increase exposure to cadmium, as cigarettes contain 1-2 μg of cadmium about 10% of which is absorbed. Cadmium accumulates in the liver and kidneys, which account for 50% of the body burden, and is excreted in the urine.

Biological monitoring

- Blood cadmium reflects average intake over the previous few months.
- Urine cadmium is indicative of body burden when exposure is low to moderate.

Sample requirements

6 mL random urine. Ensure that hands are washed and clothes are free of contamination.
To minimise contamination of the sample with cadmium from tobacco, the sample should be collected in a smoke free environment. Sampling time is not critical.
Note: some yellow top specimen collection containers have been shown to be contaminated with cadmium.

For occupational monitoring it is suggested that both blood and urine is collected.

Chromium in Plasma and Whole Blood

Chromium is an essential trace element necessary for metabolism of carbohydrates and fats. In serum Chromium occurs as Cr^{III} and is bound to serum proteins particularly transferrin and albumin. Chromium (III) is essential for insulin activity and has a low toxicity compared to Chromium (V). Low levels of chromium are widely distributed throughout the body with no special concentration in any particular tissues. Inorganic chromium is poorly absorbed, however chromium in natural complexes such as brewer's yeast are better absorbed.

When chromium enters the bloodstream it is taken up by the red cells and converted to Cr^{III}, it then rapidly disappears from the bloodstream into the tissues. Blood and tissue chromium are not in equilibrium therefore analysis of blood chromium is not a good indication of exposure. Chromium is absorbed through the digestive tract, respiratory tract and skin and is rapidly excreted principally in the urine. Urinary chromium measurement is used as an indicator of occupational exposure.

Plasma chromium is not a good indicator of occupational exposure and is not measured routinely for monitoring. Increased plasma chromium is sometimes seen in patients with metal on metal hip replacement when degradation and wear of the prosthetic joint has occurred and metals ions accumulate in the surrounding tissues and enter the bloodstream. Increased levels are also seen in patients on dialysis as chromium is included in the dialysis fluid.

Interpretation of Results

Biological Reference Interval: 1 - 20 nmol/L (Plasma and Whole blood)

Patients with metal on metal hip replacements routinely show a plasma chromium level 2-3 times the non-exposed reference interval.

Management recommendations for patients with metal on metal hip replacement implants:-
Plasma or blood chromium level >135 nmol/L(7ug/L (ppb))
Plasma or blood cobalt > 119 nmol/L(7ug/L(ppb))
Indicate potential soft tissue reaction.
Ref: Medicines and healthcare products Regulatory Agency (UK) MDA/2012/008

Sample requirements

6 mL K2 EDTA (Royal Blue) whole blood.
The plasma should be separated from the red cells within 4 hours of collection, aliquot 1 mL plasma, refrigerated 4°C.
For occupational monitoring it is suggested that urine is collected, not blood.

Chromium in Urine

Introduction

Chromium is an essential trace element necessary for the metabolism of carbohydrates and fats. In chromium deficiency a condition similar to diabetes is exhibited. Natural complexes that include chromium (e.g. brewer's yeast) appear to be better absorbed from the GI tract than inorganic salts of chromium. Chromium enters the blood stream and is converted to chromium$^{(III)}$ and is rapidly taken up in the tissues. As the tissues and blood are not in equilibrium with regards to chromium, the blood level is not a good indicator of chromium stores. About 80% of absorbed chromium is eliminated in the urine, (1/2 life 15-41 hours) so that urinary chromium levels can be used as an indication of body burden.

Chromium can also be absorbed through the lungs from chromate fumes and dust. Chromium exists in two main valency states, trivalent and hexavalent. Chromium$^{(VI)}$ is better absorbed and more toxic than chromium$^{(III)}$, and has also been listed as a carcinogen implicated in lung cancer. If absorbed $Cr^{(VI)}$ is not converted to $Cr^{(III)}$ in the red blood cells, acute kidney damage can occur.

Occupational exposure to chromium occurs in wood tanalising, stainless steel welding, chrome plating, the leather tanning industry and the use of lead chromate or strontium chromate paints.

Sample requirements

6 mL random urine. Post shift – The last two hours to immediately following the end of the working day & End of Work Week – After at least 4 days of exposure. Ensure that hands are washed and clothes are free of contamination.

Toxic effects

The toxic effects of chromium are largely caused by the highly corrosive nature and solubility of chromate compounds used in industry.

Skin:

Skin contact causes allergic reactions and sensitisation. 'Chrome Burn', where the skin is broken, may lead to increased absorption and possible kidney damage.

Inhalation:

Acute inhalation of chromium fumes causes coughing, wheezing and fever may lead to kidney damage. The chromium$^{(VI)}$ compounds of low solubility are recognized as carcinogens from exposure by inhalation leading to lung cancer. Perforation of the nasal septum and chronic bronchitis are also consequences of chromium inhalation.

Urine chromium is used in occupational monitoring.

Cobalt in Plasma and Whole Blood

Introduction

Cobalt is an essential trace element and is utilised as a component of B12. Cobalt is absorbed by inhalation and ingestion and the amount absorbed depends on the solubility. Soluble compounds are easily absorbed and excreted in the urine. Due to the low level of cobalt in body fluids urine cobalt is used as a measure of occupational exposure. Non-occupational exposure to cobalt can be the result of dental prosthesis and joint replacement. In this case plasma cobalt measurement may be of use.

Interpretation of Results

Biological Reference Interval : 1 - 12 nmol/L (plasma and whole blood)
Patients with metal on metal hip replacements may show results 2-3 times non-exposed levels.

Management recommendations for patients with metal on metal hip replacement implants:-
Plasma or blood chromium level >135 nmol/L(7ug/L (ppb))
Plasma or blood cobalt > 119 nmol/L(7ug/L(ppb))
Indicate potential soft tissue reaction.
Ref: Medicines and healthcare products Regulatory Agency (UK) MDA/2012/008

Sample requirements

6 mL K2 EDTA (Royal Blue) whole blood.
The plasma should be separated from the red cells within 4 hours of collection, aliquot 1 mL plasma, refrigerated 4°C.

Cobalt in urine

Introduction

Cobalt is a naturally occurring element widely distributed in the environment, it is an essential trace element and is utilised as a component of B12. Cobalt is absorbed by inhalation and ingestion and the amount absorbed depends on the solubility, soluble compounds are easily absorbed and rapidly excreted in the urine. Due to the low level of cobalt in body fluids urine cobalt is used as a measure of occupational exposure.
Occupationally cobalt is used as an alloy in the production of hard metal (tungsten carbide), manufacture of high temperature alloys for jet engines, in magnets and as a catalyst in after burners. It is also used as an alloy in joint prostheses. Workers in the Sawdoctor and Knifegrinder industries are at risk from inhalation of cobalt from the dust created during grinding processes.

Sample Requirements

6 mL random urine. Post shift – The last two hours to immediately following the end of the working day & End of Work Week – After at least 4 days of exposure. Ensure that hands are washed and clothes are free of contamination.

Toxic effects

Inhalation of cobalt compounds can cause cobalt sensitisation, occupational asthma and interstitial lung disease associated with high exposure, previously called ‘hard metal’ disease. Cobalt may also cause allergic dermatitis.

Copper in Plasma

Clinical Background

Copper

Copper Metabolism:	Intake	- dietary	3.2 mg/day food 0.4 mg/day water
	Output	- excreted through bile (≅ 80%) - excreted by the kidneys (≅ 4%)	

Copper is absorbed from the small intestine. It is stored in the body in bone marrow and other tissues. Most of the serum copper is bound to Caeruloplasmin, the rest is loosely bound to Albumin. Copper can also bind to Transferrin (raised Cu levels can be found in Fe deficiency anaemias). Copper also has biological functions associated with enzyme activity; uricase, the monoamine oxidases, ascorbic acid oxidases and tyrosinase.

Women of child bearing age have higher Copper levels than men (Oestrogen therapy leads to levels of up to 47 µmol/L). Newborn infants have lower serum Copper levels ≅ 3 – 9 µmol/L.

Increases of serum Copper can be seen in a variety of disorders (usually as a result of increases in caeruloplasmin levels) e.g. sub-acute and chronic infections, acute leukaemia, aplastic anaemia, heamochromatosis and in Hodgkins disease where a response to treatment can be judged by a fall in serum Copper levels (often to normal levels)

Urine Copper is increased in proteinurias and nephrosis and Wilson's disease.

Low serum Copper levels occur when there is poor synthesis of proteins, or dietary lack or absorption is impaired.

Copper is of particular interest in Wilson's disease and Menkes syndrome.

Wilson's disease is a copper storage disease in which Copper is unable to bind to caeruloplasmin. There is an increase in the amount of Copper absorbed from the diet which then becomes deposited in the tissues, particularly the liver and brain (leading to gross mental deficiency). Treatment is by chelation with agents such as penicillamine.

In Menkes syndrome (kinky hair disease) dietary Copper is unable to pass through the gut mucosa, serum Copper levels are very low, as is the urine Copper level.

Interpretation of Results

Biological Reference Interval

Plasma Copper

Age	Male	Female	
0-1	1.4 - 7.2	1.4 - 7.2	µmol/L
1-5	12.6 - 23.6	12.6 - 23.6	µmol/L
6-9	13.2 - 21.4	13.2 - 21.4	µmol/L
10-14	12.6 - 19.0	12.9 - 18.9	µmol/L
15-19	10.1 - 18.4	11.3 - 25.2	µmol/L
19+	11.0 - 20.0	11.0 - 22.0	µmol/L

Oestrogen therapy increases the copper reference range to 11.0-35.0 µmol/L.

Sample requirements

6 mL K2 EDTA (Royal Blue) whole blood.
The plasma should be separated from the red cells within 4 hours of collection, aliquot 1 mL plasma, refrigerated 4°C.

Copper in Urine

Introduction

The most common disorder involving mineral metabolism is Wilson's disease or hepatolenticular degeneration. This is an autosomal recessive disorder, the frequency being of the order of 1 in 100,000 live births.

The two fundamental disturbances of copper metabolism in Wilson's disease are:
Gross reduction in the rate of incorporation of copper into caeruloplasmin
Considerable reduction in biliary excretion of copper

Copper accumulates in the liver, causing progressive liver damage and subsequently overflows into other tissues, especially the brain. The classical presentation is of adults with progressive neurological symptoms, low serum concentrations of copper and caeruloplasmin, raised urinary copper excretion and characteristic copper deposits in the corneas (Kayser-Fleischer rings). Children and adolescents frequently present with a variety of hepatic symptoms including hepatic failure.

Note: It is always advisable to measure serum copper or caeruloplasmin levels, urinary copper excretion and liver copper (see Iron and Copper in Liver tissue) in the diagnosis of Wilson's disease.

The possibility that a raised urine copper may be due to contamination should be excluded. Ensure that an acid washed bottle was used for collection, the sample was collected cleanly into the acid washed bottle and an aliquot was taken prior to measurement of urine volume.

Sample requirements

6 mL random urine.

Measuring urine copper for occupational exposure is not recommended as there are no work place exposure standards.

Fluoride in Urine

Introduction

Industrial exposure to fluoride occurs in the manufacture of superphosphate, where phosphate rock (which contains small amounts of fluoride) is crushed and dried, releasing fine particles of fluoride dust. Fluoride is also released as an impurity in the production of aluminium. Workers are monitored to prevent osteofluorosis.

Interpretation

An acute dose of fluoride is rapidly excreted in the urine with a half life of a few hours.

Non exposed levels 0 - 31 µmol/L

Workplace Exposure Standards (2019)

- Pre shift Biological Exposure Index 105 µmol/L (2 mg/L)
- Post shift Biological Exposure Index 160 µmol/L (3 mg/L)

- *Biological Exposure Index (BEI) - levels above which excessive exposure has occurred..*

If the post-shift level is exceeded, a pre-shift sample should be taken at the beginning of the shift 48 hours after previous exposure, and another post-shift sample taken at the end of the working week.

The pre-shift sample reflects the body (skeletal) burden of fluoride while post-shift samples reflect exposure.

If the pre-shift sample and repeat post-shift samples exceed the BEI level then dietary (tea and coffee) intake and work practices need to be evaluated.

Sample Requirements

6 mL random urine. Pre shift – Following a period of 16 hours with no exposure and Post shift – The last two hours to immediately following the end of the working day. Ensure that hands are washed and clothes are free of contamination.

Iodine in Urine

Introduction

Iodine is an essential trace element and its primary source is mainly seaweed and fish. A deficiency of iodine intake could lead to disorders like goitre and cretinism.

The most widely used marker for iodine deficiency is the measurement of a 24-hour urine urinary iodine excretion. This is because more than 90% of the body iodine is excreted in urine and thus reflects the iodine intake.

Iodine intake in New Zealand appears to be dropping and some of the contributing factors to an iodine-deficient diet are:

- A reduced intake of iodised salt in cooking, due to the introduction of the microwave oven
- A positive response to health guidelines
- The phasing out of the use of iodophor cleaning detergents in the dairy industry
- Reduced fish intake

Sample Requirements

A 24-hour urine is required to assess the iodine status of an individual. Store at 4ºC until analysis.
Send 6 mL of the mixed urine to the laboratory for analysis.

Interpretation of Results

A 24 hour urine is required to assess the iodine status if an individual. The recommended dietary intake of iodine is 1.2 µmol/day for males (150 µg/day) and 0.95 µmol/day for females (120 µg). Up to 75-90% of dietary iodine is excreted in the urine.

The reference range in adults is 0.2 – 5.0 µmol/L
and in children is 0.3 – 6.0 µmol/L

Range derived from an iodine-replete population (Soldin etal; Clin Chim Acta 2003; 328; 185-90).

Note that urine iodine concentration is a marker of recent intake and does not necessarily confirm insufficiency.

Iron in Urine

Iron is one of the most abundant elements on earth and is essential for the existence of all plants and animals. In humans 65-70% is found in haemoglobin, 4% in myoglobin and less than 1% in other iron containing enzymes and proteins. The remaining 25-30% is stored.

Iron is not normally excreted but is continually recycled by the reticuloendothelial system from old red cells into new ones. There is a daily loss of about 1 mg of iron per day due to shedding of mucosal and skin epithelial cells and loss of small numbers of erythrocytes in urine and faeces.

Urine iron analysis is to monitor patients receiving iron chelating therapy.

Anaemia with iron overload can be seen in conditions such as sickle cell disease, thalassemia major, myelodysplasic syndromes (MDS), enzymes disorders, iron transport and storage disorders and some cancers. In these patients the iron is trapped in vital organs such as the anterior pituitary, heart, liver pancreas and joints and it is important to remove the excess iron before damage can occur. Desferrioxamine is an iron chelating agent which can be used to remove the excess iron from these patients.

Sample Requirements

A 24 hour urine collected into an acid washed bottle (available from CHL). Mix, and Aliquot and send 6 mL of the sample to the laboratory for analysis. Note measured the total volume and collection duration on request form. (prevent sample contamination).

Iron levels in urine are increased in diseases associated with intravascular haemolysis and in patients receiving chelation therapy.

Liver Biopsy Sample - Copper and Iron

Principle of Method

Copper and iron are measured in liver biopsy samples using ICP-MS. The samples are received frozen, or already dried, wrapped in tin foil. They must be dried to constant weight, the sample weight obtained, and then digested with concentrated nitric acid to break down the tissue and form a homogeneous solution. Following digesting, the samples are made up to constant volume with Water 1 and assayed as soon as possible.

Specimen Requirements

Liver biopsy received wrapped in aluminium foil in clean specimen pottle. They should be frozen on arrival and kept frozen.
Recommended sample type

Liver biopsy's can also be received mounted in paraffin blocks (as Histological specimens).

Interpretation of Results

Biological Reference Range for Liver Iron

	µg/g dry weight			mean
Normal	350	-	1250	795
Alcoholic liver disease	350	-	2450	1380
Haemochromatosis (heterozygous)	3000	-	14400	8710
Haemochromatosis (homozygous)	3000	-	67500	35200

Biological Reference Interval for Liver Copper

	µg/g dry weight	mean
Normal	<50	27
Wilsons Disease	>250	

Protocol for Liver Iron or Copper Collection

The test provides diagnostic information in cases of suspected haemochromatosis and Wilson's Disease.

A liver biopsy of >1.5 cm long is required and after biopsy should immediately be placed on a 5 cm square of aluminium foil. The foil is then folded like an envelope and placed in a urine pottle for transport to the laboratory.

On receipt in your laboratory the aluminium foil should be slightly opened and dried at

37oC for 24 hours. After drying the foil should be tightly closed and may be sellotaped to the referral letter or request form. Drying of the sample will prevent bacterial growth and protect the liver sample from contamination by environmental iron and copper. (Alternatively the sample in aluminium foil should be frozen and sent to the Laboratory on ice).

Brief clinical details should be included plus ferritin, iron and %saturation levels in cases of suspected haemochromatosis.

Lead in Blood

Introduction

Lead is used in storage batteries, ammunition and type metal, cable sheaths, solder, previously used in anti-knock compounds in petrol and the plastics industry. It is also present in many metals such as brass (1-3.5%). Lead can also be a problem in the home, particularly from sanding old lead based paints and making diving and fishing weights, and in artists' studios and potteries. Indoor small bore rifle shooters are also at risk from lead poisoning.

Acute lead poisoning in adults is commonly characterized by abdominal pain, tiredness, aching limbs and joints, and irritability. Nerve palsy and wrist drop have also been mentioned but are very rare. In children and animals lead poisoning is accompanied by CNS signs such as convulsions, irritability, vomiting and anaemia. High lead intake can also be asymptomatic as in a lot of occupational exposure where increased lead intake is seen only by blood lead level measurement. Chronic cases present in neurological wards with polyneuritis and renal impairment.

Sample requirements

6 mL K2 EDTA (Royal Blue) whole blood.

Interpretation

Non occupational exposure

A whole blood lead of > 0.48 μmol/L (10 μg/ml) is a notifiable disease to the local Public Health Units. Testing laboratories must refer these results to the Department of Health

Results greater than 0.48 μmol/L are abnormal; they are indicative of increased lead absorption and should initiate environmental measures to minimise the level of exposure.
Between 1.0 and 1.9 μmol/L some children will require chelation therapy and a paediatric consultation is recommended. Above 1.9 μmol/L most children will require chelation and referral to a paediatrician is highly desirable. Levels above 3.0 μmol/L generally require URGENT medical treatment to reduce the risk of lead encephalopathy.

Occupational exposure

It is desirable for all lead workers to minimize their exposure to lead and maintain a whole blood lead level less than 0.97 μmol/L. It is the responsibility of the employer to ensure regular monitoring of blood lead levels.
Biological Exposure Limits (BEI)for blood lead are;

- A BEI of 0.97 umol/l(20ug/dL) of whole blood
- A suspension (removal) level of 1.45 umol/L (30 ug/dL)of whole blood for all males and females not of reproductive capacity.

- A suspension (removal) level of 0.48umol/L (10 ug/dL) of whole blood for females of reproductive capacity and those pregnant/breast feeding.
- Ideally pregnant women or those planning to become pregnant should have no exposure to lead at all. This is because the developing foetus is extremely susceptible to lead.

Ref;Workplace Exposure Standards and Biological Indicies 11th ed.2019

Biological Monitoring of Lead Workers

The aim of blood lead monitoring of workers exposed to lead is to maintain a blood lead level below 0.97 μmol/L of whole blood. A pre employment screen is recommended to exclude sources of lead other than occupational exposure; these may include home renovations, small bore rifle shooting, casting lead sinkers, home mechanics etc.

New employees in 'at risk' occupations should be monitored monthly until the blood lead level is stabilised. After that monitoring at regular intervals is recommended;

< 1.5 μmol/L whole blood lead	repeat 12 monthly
1.5 – 1.9 μmol/L whole blood lead	repeat 6 monthly
2.0 - 2.3 μmol/L whole blood lead	repeat 3 monthly
≥ 2.4 μmol/L whole blood lead	repeat fortnightly until the level has decrease to 1.93 μmol/L or less.

Occupations at risk of lead exposure

High risk:
Majority of workers with whole blood lead > 1.5 μmol/L

Radiator repair	Smelting
Muffler repair	Scrap metal
Foundry (general)	Container repair
Engine reconditioning	Small bore rifle shooting
Paint removal (with lead based paints)	Lead battery manufacture

Medium risk:
Majority of workers with whole blood lead > 0.9 < 1.5 μmol/L

Panel beating	Metal extrusion
Metal machining	Garage mechanic
Pottery/ceramics	Metal polishing
Gas cutting/welding	Lead casting
Spray painting	Plastic production

Low risk:

Majority of workers with whole blood lead < 0.9 μmol/L

Plumbing	Boat building
Cable jointing	Bright soldering
Car assembly	Petrol pump attendant
Electroplating	Exhaust fume exposure

Sources of lead for different occupational groups

Radiator repair:
Solder (60% lead, 40% tin) is used. After repair the excess solder is buffed off using a grinder type wheel, creating dust. In addition radiators were formerly painted with lead based paint but this practice has been discontinued.

Smelting:
High heat generated in the furnace leads to fumes. Lead (2-3%) is added to brass (copper/zinc alloy) and some bronzes (copper/tin alloy) e.g. gunmetal, as it gives the metal a lubrication quality and prevents machinery seizure. Phosphor bronze and aluminium bronze have minimal lead content.

Muffler repair:
Exhaust systems may have deposits of lead oxide from lead petrol. This creates fine dust and lead fumes during welding.(Mostly seen in older vehicles)

Scrap metal:
This includes burning off the covering of old cables, cutting lead enamelled baths, handling old lead batteries and smelting down lead using crude furnaces.

Metal moulding:
The high temperatures used produce fumes from lead and lead containing alloys.

Container repair:
Welding, brushing and sandblasting of lead paint in the confined spaces of containers produces dusts and fumes.

Engine reconditioning:
This involves engines and oils that may be contaminated with lead deposits from leaded petrol.

Panel beating:
Workers are exposed to lead dust and fumes from sanding and welding car bodies containing lead. Lead is still used by some panel beaters to repair surface defects.

Metal machining:
Dust is created by the cutting and spinning of metal alloys containing lead.

Metal polishing:
Fine dust is created when buffing lead based alloys.

Printing:
Old printing equipment used lead based letters for printing.

Welding/gas cutting:
This involves cutting metals coated with lead based paints or bath enamel.

Spray painting:
Exposure occurs during the preparation of surfaces previously coated with lead based paints.

Lead battery manufacture:
Used lead batteries are recycled by smelting down and making lead ingots. Manufacture of new lead batteries involves making the lead plates, pasting them with a lead oxide paste and assembling the battery.

Plastic production:
PVC contains tri basic lead sulphate as a scavenger of acids produced in the degradation of PVC and improves thermal stability. Workers are exposed in the debagging room, where the dampened powder is opened and mixed with high speed mixers and a free flowing powder is formed which contains approximately 2% lead. A fine dust can escape from the mixers.

Leadlighting:
Soldering temperatures are generally not high enough for the fumes to be hazardous. However, lead dust is created when sanding and buffing the lead solder seams.

Metal extruding:
See metal moulding.

Garage mechanic:
See engine reconditioning.

Pottery/ceramics:
Lead based glazes are used.

Plumbing:
Plumbers sometimes use red lead putty as a sealant, as well as soldered joints and lead flashings.

Cable jointing:
Lead is used to mould around joins in cables, which is generally carried out in confined spaces. This practice is gradually being phased out in favour of plastics.

Electroplating:
Lead soldered seams are buffed up and polished prior to chrome plating.

Bright solder/electronics:
These use lead solder. Jewellers mostly use silver solder (bright solder).

Paint removal/painting and decorating:
Exposure occurs during removal of lead based paints, eg by sanding.

Exhaust exposure/petrol pump operation:
Leaded petrol exhaust fumes affect car park attendants and WOF workers.

Smallbore rifle shooting:
Lead fumes arise from both the bullet and the primer. There is additional lead in the dust when cleaning the shooting range.

Lead in Urine

Introduction

Lead is excreted via the kidneys and the faeces. Measurement of urine lead is used most commonly to follow lead excretion of patients on chelation therapy for lead poisoning.

Urine lead is also measured to indicate exposure to tetra-alkyl (organic) lead which was used up until October 1996 as an antiknock agent in petrol. Excessive exposure to petrol is unlikely to lead to high urine lead levels.

Sample requirements

6 mL random urine. Ensure that hands are washed and clothes are free of contamination.

Manganese in Whole Blood

Introduction

Manganese is an essential micronutrient found throughout the body, with the highest levels found in the liver. It accumulates in tissues high in mitochondria

and is a cofactor in enzymes such as hexokinase, superoxide dismutase and xanthine oxidase. Manganese is associated with bone and tissue formation, carbohydrate metabolism, reproductive processes and lipid metabolism. Manganese is absorbed through the gastrointestinal tract with absorption being similar to iron absorption. Manganese is mainly excreted in bile with only a small amount excreted in urine. The human requirement for manganese is very low and even during prolonged TPN no clear evidence of deficiency has been documented. However because of the potential importance of manganese, additives containing it have been included in TPN regimens.
The concentration of whole blood manganese is about 10 times higher than in serum therefore the manganese from contamination is proportionately less significant, eliminating some sampling precautions. Whole blood manganese may better reflect manganese stores in tissue therefore it is recommended to use whole blood samples for assessment of manganese status and long term occupational exposure. Manganese is used in iron, steel and battery production industries. Occupational exposure to manganese is through the lungs via inhalation during mining of manganese ores and welding of mild steel (used as a toughening agent). Permanganate compounds are used in glass and ceramics industries and are also used as powerful oxidising agents.

Toxic effects

Exposure to high levels of manganese can cause non-specific symptoms and signs of neurological deterioration including irritability, apathy asthenia, headaches, lethargy and weakness in the extremities and in a few cases can lead to Parkinson's disease. These symptoms are believed to arise due to excess manganese deposition in the basal ganglia which can be seen as hyper-intense areas on MRI of the brain.
Manganese toxicity has also been documented in patients on long term TPN who are particularly at risk if there is liver dysfunction. Increased whole blood manganese has also been reported in liver disease, rheumatoid arthritis and iron deficiency anaemia. Neurological effects exhibit Parkinson like symptoms, including behavioral and emotional disturbances, if diagnosed in the early stages these effects can be reversed. Some haematological changes may also be observed, such as greatly reduced white cell count (leucopoenia) and lymphocytosis, or an increase in haemoglobin count. However in some cases there may be no changes at all.

Sample requirements

6 mL K2 EDTA (Royal Blue) whole blood.

Mercury in Urine

Introduction

Mercury, commonly called quicksilver, is a heavy, mobile liquid metal and is slightly volatile at room temperature. The vapour is readily absorbed through the lungs. Sources of mercury include metallic vapours, mercury salts and the more toxic organic mercury compounds. Metallic mercury (used in gold mining) is particularly dangerous due to mercury vapour being absorbed via the respiratory tract. This danger is increased further when the mercury is heated.

Mercury and its inorganic salts are used in a variety of ways. These include disinfectants, antiseptics and insecticides, and in scientific instruments and processes. Mercury is also used for extracting gold and silver from ores. Organic mercurials are found as antifungal preparations. A continuing source of exposure to mercury which has become a cause for concern is that of dental nurses who use amalgams for fillings in teeth. However, due to advances in dental surgery hygiene and the use of different types of fillings, this is not as significant a problem as it was 15 years ago. Methyl mercury, which is highly toxic, is found in fish and is a major cause for concern in badly polluted waters.

Mercury and its salts can enter the body by inhalation, oral ingestion or absorption. Mercury vapour cannot be absorbed through intact skin but many mercurial compounds can be. It is very toxic and cumulative. In the blood inorganic mercury is found equally in the plasma and red cells, while the alkyl compounds, such as methyl mercury, are concentrated ten to twenty fold in the red cells. The main target organs for mercury are the central nervous system and the kidney. Mercury is excreted in the urine (inorganic and metallic)and faeces(organic) and has a half life in the body of about 70 days. Increased exposure intensifies the symptoms.

Low grade continuous exposure can lead to:

- Inflammation of the mouth, soft gums, loose teeth, excessive salivation, metallic taste and foul breath.
- Tremor (hatter's shakes), particularly when the person is being observed or is in an unfamiliar environment or job.
- Mental and nervous symptoms including behavioural changes, stammering, anxiety, loss of sleep and loss of energy and drive.

Sample requirements

6 mL random urine. Ensure that hands are washed and clothes are free of contamination.
The sample needs to be frozen and sent to the laboratory frozen.
Sampling time is not critical

The reported manifestations of subacute mercury poisoning are primarily neurological, with tremors, vertigo, irritability, moodiness and depression. They are associated with salivation, stomatitis and diarrhoea.

Mercury in whole blood

Blood mercury is mainly measured to detect exposure to organic (methyl) mercury from environmental exposure. Micro organisms in water methylate inorganic mercury thereby introducing organic mercury into the food chain. Organic or methyl mercury in found in both freshwater and saltwater fish, particularly in badly polluted waters. Human dietary exposure is mainly by eating fish.
In blood inorganic mercury is equally distributed between the plasma and red cells, however organic compounds are concentrated ten to twenty fold in the red cells hence whole blood mercury is mainly a measure of organic mercury. Excretion is mainly via faeces and has a half life of approximately 70 days. Dental filling exposure is from inhaling the vapour of elemental mercury and is typically slight.

Low grade continuous exposure can lead to;
Inflammation of the mouth ,soft gums, loose teat , metallic taste and foul breath.
Tremors, metal and nervous symptoms including behavioural changes.

Sample requirements

6 mL K2 EDTA (Royal Blue) whole blood.

Molybdenum in Urine

Introduction

Molybdenum is an essential trace element used as a co factor for enzymes such as xanthine oxidase, which is involved in the degradation of purines to uric acid. The human requirement for molybdenum is extremely low and deficiency is rare.
In ruminant animals high molybdenum from grazing interferes with copper absorption, causing anaemia, stunted growth and bone deformities, sheep also show degeneration of the central nervous system.
Occupationally molybdenum is used in alloys as a hardener for steels and superalloys, used in turbine wheels and jet engines; they can contain as much as 30% molybdenum. It is also used in the production of some ceramics including joint prostheses, pigments and electrical wire. Its compounds are also used as catalysts and in lubricants. Small amounts are sometimes added to fertilizer as in some plants it is necessary for nitrogen fixation.
Molybdenum is absorbed through the gastrointestinal tract and is rapidly excreted in the urine.

Toxicity
Reports of toxicity are rare.
Exposure to molybdenum trioxide during production of compounds at high temperatures has been reported as causing irritation to the mucous membranes, headaches and aching joints. After high exposure uric acid and ceruloplasmin were slightly increased.
In Armenia where soil concentration is high an increase in gout-like symptoms have been reported.

Sample requirements

6 mL random urine. Post shift – The last two hours to immediately following the end of the working day & End of Work Week – After at least 4 days of exposure. Ensure that hands are washed and clothes are free of contamination.

Nickel in Urine

Introduction

Nickel is relatively non toxic essential trace element. It is important in the metabolism of cell membranes and is found in significant concentrations in RNA & DNA. Nickel is poorly absorbed from the diet and is mainly excreted in the faeces, with small amounts being excreted in the sweat and urine. However, when excess nickel is present in the system due to occupational exposure the amount excreted in the urine increases. Urinary concentration is therefore used as an index of exposure. Nickel has a half life of 17-39 hours.

Occupational exposure occurs in nickel plating, with different alloys being used in the manufacture of stainless steel, coins, nickel chrome resistance wire, magnets and silver cutlery. Nickel carbonyl is the gas formed in the nickel refining process when carbon monoxide reacts with nickel. It is the basis for the Mond process, in which objects are coated with nickel of very high purity. Nickel fumes are also given off during gas cutting or stainless steel welding.

Sample requirements

6 mL random urine. Post shift – The last two hours to immediately following the end of the working day. Ensure that hands are washed and clothes are free of contamination.

Interpretation

Non exposed levels	< 0.4 µmol/L
Mild exposure	1.7 - 8.5 µmol/L
Severe exposure	> 8.5 µmol/L

Toxic effects

Nickel carbonyl gas is the most toxic form of the element, causing dizziness, headache, fever and acute breathing problems. Nickel has also been implicated in nasal and lung cancer.

Contact dermatitis, or ‘nickel itch’ is common in individuals dealing with nickel compounds, even in wearing of jewelry and metal domes on clothing.

Ref; Zenz C, Dickerson OB and Horvarth EP (Eds). *Occupational Medicine. Third*

Edition. Mosby, London. 1994

Selenium in Plasma

Introduction

Selenium levels in South Island soils are particularly low and regular supplementation of livestock occurs to prevent deficiency symptoms, such as white muscle disease and failure to thrive. Similarly, humans living in this area have low plasma selenium levels by world standards, although obvious deficiency has only rarely been reported in New Zealand. Selenium is an important component of glutathione peroxidase and is thus implicated in defences against oxidative damage. Selenium deficiency has been implicated in the development of cot death, cardiovascular disease, including heart failure and coronary artery disease, and cancers.

Severe selenium deficiency results in Keshan disease (heart failure) in several provinces of China but has now been eradicated by supplementation of the population. Finland, also, has adopted a policy of national selenium supplementation. Deficiency may be particularly severe in the new-born.

Sample requirements

6 mL K2 EDTA (Royal Blue) whole blood. The plasma should be separated from the red cells within 4 hours, aliquot 1 mL plasma, refrigerated 4°C.

Plasma selenium levels reflect recent ingestion of selenium and are a good indicator of acute and chronic poisoning. During deficiency plasma selenium levels generally reflect plasma glutathione peroxidase levels but at higher concentrations this relationship is lost.

Selenium in Urine

Introduction

Selenium is used to supplement livestock feed and in some fertilisers. It is also used in the electrical and electronics industry, semiconductors, glass production, and the paint industry. The cosmetic industry uses selenium in antidandruff shampoos.

Sample requirements

6 mL random urine. Post shift – The last two hours to immediately following the end of the working day. Ensure that hands are washed and clothes are free of contamination.

Interpretation

No Biological Exposure Index is given for urine selenium, however urine selenium levels may be used to confirm absorption but the relationship to exposure has not been established. For occupational monitoring a maximum level of 1.3 µmol/L (100 µg/L)[7] has been recommended.

To ensure adequate assessment of exposure to selenium, urine samples must be collected at the end of the working shift. Urinary concentrations rise dramatically with a sudden increase in ingestion of selenium and can be used to differentiate between acute and chronic exposure.

Silver in Plasma

Introduction

Silver is a rare element occurring naturally as a pure metal and in ores. It is released into the air and soils through natural weathering and through the processing of ore, steel refining, combustion of fossil fuels and incineration of municipal waste. The main industrial use of silver has been in the photographic industry. The general population is exposed to silver through ingestion of drinking water and food. Foods with high silver content include seafood from areas near sewerage outflows and industrial sources and crops grown in areas with high ambient soil levels.

Occupational exposure occurs in the primary metal industries, air conditioning and refrigeration mechanics, plumbers, welders, and those involved in processing silver nitrate and oxide for use in the photography, smelting and refining industries. Absorption is either through inhalation or oral ingestion or dermal absorption. Bioaccumulation occurs in filter feeding seafood, but reliable data on food-chain bioaccumulation is not available. Little data is available on exposure levels in humans.

There are no known acute effects of exposure to silver metal; but some silver compounds, such as oxides and nitrates, are irritants. With chronic exposure silver binds to sulphhydryl groups on proteins and can lead to darkening of the skin, particularly sun exposed skin (argyria), and deposition in the cornea (argyrosis). Nephrotoxicity has been reported. Elimination is primarily through the faeces.

Plasma silver levels are an indicator of recent exposure irrespective of the route.
Silver acts as an antibacterial agent and silver infused dressings are often used to treat some skin conditions and treatment of burns.
Colloidal Silver is sometimes taken as a medicine which if taken excessively will increase the plasma silver levels.

Urine silver is a less reliable indicator of exposure, (in a study by DiVincenzo[13] – 100 % of exposed workers had faecal silver above the limit of detection, but only 6 % of urine samples had detectable silver). Intermediate and long-term exposure to silver may be determined by monitoring plasma silver levels or from skin biopsy.

Specimen Requirements

6 mL K2 EDTA (Royal Blue) whole blood. The plasma should be separated from the red cells within 4 hours, aliquot 1 mL plasma, refrigerated 4°C.

Thallium in Urine

Introduction

Thallium is a soft heavy metal found as a by-product from smelting copper, lead or zinc. Thallium is used in small quantities in the manufacture of optical lenses, imitation jewellery, in dyes and pigments and thallium sulphate is used as a rodenticide.
Thallium is absorbed through inhalation, ingestion and through the skin. In the blood it is mainly bound to the red cells and is excreted by the kidneys. Thallium compounds are highly toxic cumulative poisons. Large doses cause gastrointestinal symptoms such as vomiting and diarrhoea followed by hypotension and brachycardia initially then followed by hypertension and tachycardia. Severe cases lead to muscle paralysis and cardio respiratory failure.
Chronic poisoning causes peripheral neuropathy, gastroenteritis and characteristically, loss of hair.

Specimen requirements

6 mL random urine. Post shift – The last two hours to immediately following the end of the working day & End of Work Week – After at least 4 days of exposure. Ensure that hands are washed and clothes are free of contamination.

Tin in Urine

Introduction

Tin is a soft, insoluble metal extensively used in the caning industry to line food, beverage and aerosol cans. It is present in brass, bronze, pewter and solder. Tin can be combined with other elements (chlorine, sulphur, oxygen) to form so called inorganic tin, these compounds are present in toothpastes, food additives, colourants, perfumes and soaps. Organotin compounds – alkyl and phenyl derivatives – are used in the manufacture of plastic pipes, food packaging, wood preservatives, antifouling paints and rodenticides.

Normal population exposure is primarily from food and drinking water. Tin in its various forms is present in normal soils and hence vegetables. Food preserved in tin lined cans is a significant source of tin in the diet; however more than 90 % of cans are lacquered to prevent contact of food with the tin, reducing the tin content of the food from 100 ppm in unlacquered cans to 25 ppm in lacquered cans. Light coloured fruit and fruit juices are an exception being packed in unlacquered cans; the tin helps preserve the colour of the fruit. Stannous fluoride is often added to toothpaste. Seafood and drinking water may also contain tin (butyltin) as leachates from antifouling paints and PVC pipes. Occupational exposure occurs in processing industries which work with tin containing compounds, exposure is generally through inhalation of dust.

Only small amounts of inorganic tin and tin compounds are absorbed from the gastrointestinal tract and the urine is the main route for excretion. The majority of ingested tin is excreted within 24 hours but some can be retained in the bones and tissues for 2 – 3 months. Acute health effects from ingestion of large quantities of tin include abdominal pain, anaemia, hepatic and renal dysfunction. Tin absorption reduces the absorption of zinc.

Organic tin compounds (alkyl- and phenyltin derivatives) can cause a range of toxic effects after inhalation, ingestion or dermal exposure. These include skin, eye and respiratory irritation. Acute and chronic neurological problems have also been reported. Very large acute ingestions may be lethal.

Interpretation

Urinary tin levels are known to increase after acute exposure to tin and tin compounds and reflect the body load of tin and tin compounds. Levels can vary with dietary intake, hence pre and post exposure samples are recommended.

No Biological Exposure Index is available for urine tin.

Sample requirements

6 mL random urine. Pre shift – Following a period of 16 hours with no exposure. OR Post shift – The last two hours to immediately following the end of the working day.

Vanadium in Urine

Introduction

Vanadium is widely dispersed in the environment and is essential in the control of some enzyme systems in humans, eg vanadate inhibits Na^+/K^+ ATPase and Ca^{2+} ATPase and stimulates adenylate cyclase activity.

Occupational exposure to vanadium mainly occurs when fossil fuel oils rich in vanadium are burnt. The remaining ash contains vanadium, and workers who clean the boilers are at risk of exposure. Vanadium is also used in the manufacture of pigment paints and printing inks and is used in association with titanium in the manufacture of jet engines and air frames. Vanadium is excreted in the urine and levels correlate well with airborne vanadium.

Vanadium is relatively toxic at high levels, causing diarrhoea and vomiting. Dust particles cause irritation to the skin, eyes and lungs.

Sample requirements

6 mL random urine. Post shift – The last two hours to immediately following the end of the working day. Ensure that hands are washed and clothes are free of contamination.

Daily exposure can be assessed from the difference between pre and post shift urine levels otherwise collect the sample at the end of the working week.

Interpretation

Non exposed levels	< 20 nmol/L (< 1 µg/L)
	< 2.0 µmol/mol creatinine

Workplace Exposure Standards (for exposure to vanadium pentoxide)

Biological Exposure Index	110 µmol/mol creatinine

Biological Exposure Index (BEI) - levels above which excessive exposure has occurred.

Ref for exposure standards:

Guidance on Laboratory Techniques in Occupational Medicine, Ninth Edition, Health and Safety Laboratory, UK (2002).

Zinc in Plasma and Whole Blood

Introduction

Zinc is an essential trace element that is generally non-toxic and is essential for normal growth and development, wound healing and immunocompetence. It is also necessary for the activity of more than 70 metallo enzymes, e.g. carbonic anhydrase, alkaline phosphatise, RNA and DNA polymerases, thymidine kinase and carboxypeptidases.

Zinc is actively absorbed from the gut into epithelial cells, where it is stored as mucosal metallothionen or released into the plasma, where 80% is mainly bound to albumin. It is then transported to the liver, where it is stored by hepatocytes in metallothionen. Zinc is mainly stored in muscle, with bone, liver and plasma forming a small exchangeable pool. Twenty percent of body zinc is found in the skin, nails and hair.

Regulation of zinc absorption is thought to be controlled by the amount of metal free albumin. Zinc absorption decreases in the presence of dietary phytate, high dietary phosphate and excessive calcium. Coffee, dairy products and high fibre bread also reduce zinc absorption. Zinc is mainly excreted in the faeces, with small amounts being lost via the kidneys; urinary zinc increases in nephrosis, postalcoholic hepatic cirrhosis and hepatic porphyria. Increased excretion also occurs in total starvation and on administration of chelation agents. Large amounts of zinc can also be lost in sweat.

Increased zinc intake depresses copper absorption and conversely copper absorption is greatly increased in zinc deficiency. Metabolic interactions occur between zinc and cadmium, zinc and iron, and zinc and chromium. Cadmium and iron uptake are depressed by high zinc levels, while chromium and zinc are metabolised by a common pathway in the intestine and are mutually antagonistic.

In blood approximately 80% of zinc is in the red blood cells. Almost all of this is in carbonic anhydrase. About 3% is found in leucocytes, each leucocyte containing approximately 25 times the amount of zinc as each individual erythrocyte. The rest, approximately 20%, is found in the plasma. In the newborn, erythrocyte zinc levels are about half that of the adult, with levels progressively increasing until about 12 years of age.

Dietary intake: 6 mg/day for children, 2 mg/day for adults
Excretion: Bile, urine and faeces

Specimen Requirements

6 mL K2 EDTA (Royal Blue) whole blood.
The plasma should be separated from the red cells within 2-4 hours of collection due to the high level of zinc in the red cells, aliquot 1 mL plasma, refrigerated 4°C.

Red cells contain over ten times the level of zinc found in serum; haemolysed specimens are unsuitable for analysis as are samples that have sat unseparated on the red cells for long periods of time. Rubber contains zinc, thus the types of sample collection tubes used should be chosen with care.

Industrial exposure

Zinc is used in galvanising iron and steel, and as an alloy of brass and bronze. Inhalation of zinc oxide fumes produced during welding can cause metal fume fever characterised by nausea, headaches, muscular and joint pain, shortness of breath, thirst and a cough. These symptoms develop 4-12 hours after exposure and last for 1-2 days. Zinc chloride fumes, which are highly corrosive to skin, eyes and mucous membranes, are produced from welding flux, wood preservatives and the manufacture of high quality paper, dyes and deodorants. It is also used in smoke screens.

Plasma zinc levels are thought to follow a circadian pattern, with the highest values occurring in the morning at approximately 10.00 am.

Water Analysis – Na, K, Ca, Mg, Cu, Zn, Al, Pb, Fe, Cd, Cr, As, Ba, Se, Be, Ag,Tl.

Clinical Background

Regular haemodialysis is now a widely used mode of therapy for treatment of end stage renal disease. The problem of supplying water of adequate quality is critical. The specific recommendations for water treatment in any locality should be made by the physician in charge. Deionisation, reverse osmosis or a combination of both can be used. Reverse osmosis is the treatment of choice. It is a filtration-like process in which impure water is forced under high pressure against a very thin membrane made of either cellulose acetate or nylon. The membrane allows relatively pure water to pass through and retains relatively salty water.

Recommended maximum level of contaminants in the water used to prepare dialysis fluid according to AAMI (Association for the Advancement of Medical Instrumentation) guidelines. The levels quoted should not be taken as a definitive listing, but only as those which might reasonably be expected to be present and which could have clinical implications. Because sodium and potassium are present in the dialysis fluid at higher concentrations than in water, the limits quoted are those at which an increase in concentration begins to show clinical effects.

Specimen Requirements

50 mL of water sample collected into a sterile container. When collecting tap water samples, first run tap for 1 minute to flush out the system prior to collection of the sample.

Interpretation of Results

Element	Recommendations for haemodialysis systems water [1]	Drinking water standard (maximum acceptable value[2])
Sodium	3 mmol/L	8 mmol/L (200 mg/L)
Potassium	0.2 mmo/L	none
Chloride	2.8 µmol/L	7 mmol/L (250 mg/L)
Calcium	0.25 mmol/L	none
Magnesium	0.16 mmol/L	none
Copper	1.6 µmol/L	31 µmol/L* (2 mg/L)
Zinc	1.5 µmol/L	46 µmol/L (3 mg/L)
Lead	0.024µmol/L	0.05µmol/L* (0.01 mg/L)
Arsenic	67 nmol/L	0.13µmol/L* (0.01 mg/L)
Chromium	269 nmol/L	0.96µmol/L* (0.05 mg/L)
Cadmium	9 nmol/L	0.02µmol/L* (0.002mg/L)
Selenium	25 nmol/L	0.12µmol/L* (0.01 mg/L)
Iron	5.3 µmol/L	3.5 µmol/L (0.2 mg/L)
Manganese	0.9 µmol/L	7.2 µmol/L* (0.4 mg/L)
Aluminium	0.4 µmol/L	3.7 µmol/L (0.1 mg/L)
Fluoride	10 µmol/L	37-53µmol/L[#](0.7 – 1.0 mg/L)

Mercury	1 nmol/L	35 nmol/L** (0.007mg/L)
Antimony	49 nmol/L	164 nmol/L* (0.02 mg/L)
Barium	729 nmol/L	5.1 umol/L* (0.7 mg/L)
Beryllium	44 nmol/L	444 nmol/L* (0.004 mg/L)
Silver	46 nmol/L	0.92 µmol/L* (0.1 mg/L)
Thallium	9.8 nmol/L	

* MAV determinants for health significance, # For oral health ** Inorganic mercury, Ca+ Mg, 200 mg/L Water Hardness.