Selenium

Atomic number 34
Atomic weight 78.96

Collection

Whole blood	2 mL	Plastic tube - EDTA or heparin
Serum/Plasma	2 mL	Plastic tube - plain, EDTA or heparin
Urine	20 mL	Sterile Universal

Reference ranges

			Reference
Serum/plasma	µmol/L	0.75-1.46 (19-64 y) 0.66-1.57 (65+ y)	1
Blood	µmol/L	1.13-1.95	2
Urine	µmol/L	0.78 (95th percentile) 0.16-0.85 (2.5th to 97.5th percentile)	3
	µmol/24 h	0.15-0.67 (2.5th to 97.5th percentile)	4
	nmol/mmol creatinine	47.7 (95th percentile) 18.4-53.6 (2.5th to 97.5th percentile)	3,4,5

Age	Serum/plasma
Term infants (37-42 weeks)	0.26-0.88
Less than 18 mo	0.33-0.97
18 mo – 3 years	0.51-1.12
4 - 18 years	0.60-1.29

References: Adults

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Supplementary Analyses

Glutathione peroxidase

Measurement of glutathione peroxidase in erythrocytes, whole blood or plasma may be useful in some individual cases; prior discussion with the laboratory is advised.

Clinical

Selenium is an essential trace element, which serves important roles in thyroid homeostasis, antioxidant defence, and optimal immune function. There are around thirty selenoproteins, including selenoprotein P (the main selenoprotein) in plasma, glutathione peroxidase, iodothyronine deiodinase and thioreductin reductases. Some of the redox processes controlled by some selenoproteins also require vitamin E.

There is considerable interest in the association between low selenium and selenoprotein concentrations and development of various medical conditions, in particular certain cancers, brain disorders, e.g., Alzheimers, and autoimmune thyroiditis. So far however, results from supplementation trials for preventing or improving these conditions have been very variable and, for example, a recent Cochrane review concluded that there is no beneficial effect of selenium supplementation on cancer risk. Providing supplementation to critically ill patients, who typically have low plasma selenium concentrations associated with the extent of multi-organ dysfunction, has not been found to increase overall survival but data suggest a dose dependent trend. Conversely a relationship between increased selenium and selenoprotein concentrations and disordered glucose metabolism has been well described but recent evidence suggests that this is the result of, rather than the cause of, the abnormal glucose metabolism.

In food, selenium is generally found as the amino acid derivatives, selenomethionine and selenocysteine, and is present in highest quantities in brazil nuts, seafood, kidney, meat, and in American (but not European) rice and wheat. The recommended selenium intake in UK is 75 µg/day for males and 60 µg/day for females (55 µg/day in US). These intakes should result in plasma selenium concentrations of 0.95mmol/L which is thought to equate to maximal activity of glutathione peroxidase but not to optimal selenoprotein P concentrations. Selenium intakes in the UK have fallen in recent decades and are considered by some authorities to be inadequate. The safe upper limit for selenium intake is 7.5 µg/kg/day.

Deficiency

In this country selenium deficiency of livestock has occurred in the past resulting in infertility, slow growth and a degenerative myopathy (white muscle disease). For this reason pasture land is dressed with selenium.

In general, the dietary intake of selenium in man is related to the soil content of selenium where the main food crop is grown. This can range from around 30 to 50 µg/day in New Zealand to over

300µg/day in Venezuela. Hence selenium deficiency diseases can develop in specific areas around the world. For example, Keshan Disease (a cardiomyopathy) and Kashin-Beck Disease (a childhood osteoarthropathy) are well-described in regions of China and cretinism in Tibet and Central Africa where selenium intake is very low. Although the development of the disease is more complex than selenium deficiency, supplementation can eradicate these problems. Furthermore, a complex interaction exists between selenium and iodine and severe selenium deficiency may worsen hypothyroidism due to iodine deficiency while supplementation with selenium alone may lead to increased iodine losses.

Dietary selenium is absorbed mainly in the duodenum and this process is efficient (50-80%) there being no homeostatic control of GI absorption. Regulation of body content is primarily by urinary excretion. In extreme selenium deficiency urine excretion is very low and then it is only excreted in faeces. In the UK, selenium deficiency which causes overt clinical symptoms such as muscle weakness and pain is not very common and is predominantly restricted to patients with malabsorption, anorexia or poor nutrition and those on total parenteral nutrition.

There are various guidelines for supplementing and monitoring selenium in high risk groups, e.g., ESPEN Guidelines for parenteral nutrition, NICE guidelines for nutritional support in adults and BOMSS guidelines for post bariatric surgery. When assessing nutritional status, serum selenium should be measured at baseline if there is risk of depletion (e.g., severe illness, sepsis, long term nutritional support) with further testing dependent on baseline.

The increase in blood selenium following supplementation is dependent on its form - organic forms of selenium such as seleno-cysteine and seleno-methionine result in greater increases than with inorganic forms such as selenite and selenite. The organic forms have been suggested to be more advantageous in long term prevention and the inorganic forms more effective in the acute setting.

Toxicity

In addition to its essentiality, selenium can become toxic above a relatively low threshold limit.

Toxicity can occur as a result of over-ingestion of selenium supplements, ingestion of foods grown in seleniferous soils, and ingestion of foods sourced from areas exposed to industrial selenium pollution. Exposure through the workplace also occurs - the principal applications of selenium include the manufacture of ceramics, glass, photoelectric cells, pigments, rectifiers, semiconductors, and steel as well as use in photography, pharmaceutical production, and rubber vulcanizing. The severity of poisoning is variable depending on the chemical form of selenium: inorganic forms of selenium (particularly selenious acid and selenium sulphide) are more acutely toxic than organic forms (there is no evidence of toxicity with selenium-yeast).

Manifestations of acute selenium poisoning include intense irritation of eyes, mouth, nose and lungs, hypotension and tachycardia, followed by gastrointestinal upset, abdominal pain, agitation, altered consciousness, and cardio-respiratory arrest. Pulmonary oedema can also be a serious complication. Treatment following an acute selenium poisoning is supportive with the prevention of further exposure, Chelation is not recommended.

Chronic exposure causes predominantly nail changes and alopecia. Nail changes are not specific to selenosis but in a patient with increased plasma selenium concentrations, the absence of characteristic nail changes is consistent with a lack of chronic poisoning. Additionally there may be discoloured teeth, skin lesions, nausea and vomiting, fatigue, paraesthesia and poor cognitive function. There is commonly a garlic smell to the breath caused by exhalation of the volatile form, dimethylselenide. Factors that modify selenium toxicity are increased dietary protein, arsenic (which increases biliary excretion), sulphur compounds, methionine and vitamin E.

Evaluation of selenium poisoning relies heavily on clinical context and toxicity to selenium should be judged by the clinical signs/symptoms in individual subjects rather than on laboratory values. However, blood selenium concentrations <12.7 µmol/L are unlikely to be associated with serious clinical sequelae.

Acute selenium poisoning appears to occur at selenium doses >0.5 mg/kg and has been associated with serum selenium values of 5.1 – 380 µmol/L.

Mild selenosis is evident in a number of regions around the world. Studies in the USA and China indicate selenosis is associated with selenium intakes of >0.9 mg/day. Doses of up to 0.4 mg/day for shorter periods have not been associated with any ill effects. Chronic toxicity has been associated with serum selenium concentrations 6.3 – 17.7 µmol/L, although levels of <17.7 µg/L can be seen in

individuals free of toxic symptoms. A concentration of 8.3 µmol/L was found 2 weeks after a patient with alopecia, nail changes, and paraesthesia stopped taking about 7 mg/day. In a severe episode of chronic selenium exposure in a seleniferous region of China, where intake averaged 5 mg/day, symptoms of selenosis were evident when blood selenium was 12.7 – 266 µmol/L. None were noted when blood selenium was <12.7 µmol/L.

Laboratory Indices of Selenium Status

Selenium status is most commonly assessed by measurement of plasma (or serum) selenium which responds to increased or decreased intake. However, plasma concentrations are subject to the acute phase response which lowers the concentration rapidly following trauma: concentrations 40 to 60% lower than normal are found in ICU patients. This is the result of redistribution rather than a nutritional deficit. Measurement of CRP is a useful way of clarifying the cause of a low plasma selenium. Plasma selenium concentrations are age-dependent. At birth, plasma values are 40 to 70% of maternal concentrations (even lower in premature infants) and tend to fall particularly in formula-fed infants. After four to six months the concentrations rise reaching adult values in the late teens. Functional selenium deficiency can be assessed by measuring glutathione peroxidase in whole blood, red blood cells and/or plasma. Plasma concentrations correlate strongly with plasma selenium whereas whole blood and red blood cell concentrations take around four weeks to respond to changes in intake. Glutathione peroxidase activity reaches a plateau with increasing selenium intake and so this measure is not a good indicator of toxicity.

Selenium in whole blood and erythrocytes correlate with plasma levels and since concentrations do not vary during acute phase response they can be used as an indicator of deficiency in such situations. Whereas plasma concentrations change relatively quickly following changes in intake, red cell and whole blood concentrations take around four weeks to respond making them unsuitable for assessing acute toxicity.

Renal excretion is the main means of selenium homeostasis in humans and so urine concentrations are usually dependent on intake and vary within wide limits (20 to 200 µg/L). Concentrations outwith these may indicate deficiency or toxicity, although urine measurements are more variable and hence more difficult to interpret in isolation than plasma measurements. Lower urinary concentrations are found in growing children, pregnant women and the elderly. With excessive ingestion, urine concentrations can rise dramatically and rapidly so urine selenium can be useful way of monitoring selenium exposure. Urine is usually used for occupational monitoring although if it is increased, a plasma measurement should be used to evaluate the degree of selenium exposure.

In known acute selenium poisoning, measurement of plasma/serum selenium concentrations confirm ingestion and degree of absorption but may not provide a reliable indication of severity of poisoning or the prognosis. In particular it is noted that due to the redistribution of selenium in the tissues, measurements within the first hour of exposure may overestimate the degree of exposure, whereas samples taken late following exposure may underestimate it.

Although selenoprotein P has been included in a number of research studies, insufficient research has yet been carried out to indicate whether it has a role in diagnosis and management of selenium deficiency or toxicity and it is not routinely measured.

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