Chromium

Atomic number Atomic weight	24 51.99	
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
Use Trace Eleme	nts Certified	tubes

Reference ranges

			Reference
Serum/plasma	nmol/L	Less than 6	1, 2
Blood	nmol/L	Less than 15	3-6
Urine	nmol/L	8.7	7
	nmol/L	15.4	8
	nmol/24 h		
	nmol/mmol		
	creatinine		
	µmol/mol creatinine	2.85	7

References

- 1. Brune D, Aitio A, Nordberg G, Vesterberg O, Gerhardsson L. Normal concentrations of chromium in serum and urine a TRACY project. Scand J Work Environ Health 1993;**19** suppl 1:39-44.
- Torra M, Rodamit~Ns M, Corbella J, Ferrer R, Mazzara R. Blood chromium determination in assessing reference values in an unexposed Mediterranean population. Biological Trace Element Research. 1999, **70**: 183-189.
- Case CP, Ellis L, Turner JC, Fairman B. Development of a routine method for the determination of trace metals in whole blood by magnetic sector inductively coupled plasma mass spectrometry with particular relevance to patients with total hip and knee arthroplasty. Clin Chem 2001, 47: 275–280.
- 4. Cesbron A, Saussereau E, Mahieu L, Couland I, Guerbet M, Goulle. J-P Metallic profile of whole blood and plasma in a series of 106 healthy volunteers. J. Anal Tox 2013; 37: 401-405.
- Changa F-H, Wang S-L, Huang Y-L et al. Biomonitoring of chromium for residents of areas with a high density of electroplating factories. J Exposure Science Environmental Epidemiology 2006 16, 138–146.
- Sampson B, Hart A. Clinical usefulness of blood metal measurements to assess the failure of metal-on-metal hip implants. Ann Clin Biochem. 2012;49:118-31
- 7. Hoet P, Jacquerye C, Deumer G, Lison D, Haufroid V. Reference values and upper reference limits for 26 trace elements in the urine of adults living in Belgium, Clin Chem Lab Med, 2013;

51: 839-849.

8. Morton J, Leese E, Tan E, Cocker J. Determination of 61 elements in urine samples collected from a non-occupationally exposed UK adult population, Toxicol. Letters 2014; 231: 179-193.

Clinical

Chromium occurs in several oxidation states, mainly as chromium(3) and chromium(6). Chromium and chromium compounds are widely used in a number of industrial processes, such as chrome plating, pigment production, timber impregnation and photography.

Chromium is an essential trace element which, although reasonably abundant in the environment, is present in the human body in relatively small amounts. Measurement of the element is difficult in view of the low concentrations and the possibility of contamination. The intestinal absorption of inorganic chromium is about 2%, but is more bioavailable when present as an organic complex. Chromium is thought to be transported in the blood bound to transferrin.

Deficiency

Chromium deficiency was first documented in animals when it resulted in impaired glucose tolerance. Deficiency of an organic complex of chromium, the so-called glucose tolerance factor, was considered to be responsible. Glucose tolerance factor has not been isolated, but was suggested to be a complex of chromium with glutathione and nicotinic acid. Human deficiency was only revealed by the increasing use of total parenteral nutrition, (TPN) where patients presumed to be deficient in this element developed insulin resistance and neuropathy. In animals chromium deficiency has also been shown to impair growth and fertility and to be associated with hypercholesterolaemia.

The US dietary guideline for adequate daily chromium intake is $30-35 \ \mu g$ (adult male) and to $20-25 \ \mu g$ (adult female)

In clinical practice there is some evidence that diabetes mellitus and hypercholesterolaemia may be associated with chromium deficiency, and evidence that supplementation may improve these conditions. Other salts of chromium, such as chromium picolinate, have been shown to have a beneficial effect on glucose metabolism.

Toxicity

Chromium salts may have acute and chronic effects, producing both corrosive damage to mucus membranes and skin ('chrome ulcers'), and also allergic responses. A serious long-term effect is the increased incidence of malignancy in respiratory organs amongst workers inhaling chromium dust or fumes. There may also be an increased incidence of gastrointestinal tumours.

Chromium(6) is a well documented carcinogen and mutagen. Chromium is a listed envirnmental contaminant.

Surgical implants

Much of the recent clinical interest in chromium and cobalt arises from the use of a chromium/cobalt/molybdenum alloy in orthopaedic implants, especially hip replacements. Chromium and cobalt and the main components of the alloys used in many of these implants, but other metals are also present. Chromium and cobalt are primarily released from wear on metal-on-metal surfaces. The

most important of these is the surface between a metal cup in the pelvis and a metal ball. The release of metal is due to friction at the surface, which can be due to misalignment of the components and can lead to failure of the implant. If uncorrected there can be severe local tissue damage with formation of a 'pseudo tumour' and necrosis of soft tissue. There have been two warnings on these implants from the UK MHRA suggesting that patients may need to be followed up for the life of the implant. Recent evidence suggests that other surfaces may also contribute to metal release, especially the junction between the stem in the femur and the ball in modular implants. After revision surgery chromium concentrations may remain high for some considerable time due to chromium accumulation in soft tissue surrounding the implant, whereas cobalt does not accumulate.

The UK MHRA suggest that a concentration of 7 ug/L (135 nmol/L) is indicative of increased wear of the implant. Slightly lower concentrations have been proposed by other works and a European multi-disciplinary group.

In almost all patients there is no evidence of toxicity from metal release in these patients. There has been some concern about possible carcinogenicity, but evidence to date suggests that there is no increased cancer risk in these patients.

The same alloys are used in other implants, such as knee and other joints, but the hip is the only implant with a metal-on-metal surface, so the metal release is less important in these implants.

Laboratory Indices

<u>Surgical Implants</u>. Measurement of serum or blood chromium concentration is the best available index of excess exposure from surgical implantd, and concentrations may still be high some weeks after the incident. Urine chromium concentrations decline rapidly after removal from exposure, but appropriately collected samples are suitable for occupational monitoring. The MHRA advice recommends that whole blood is used for monitoring patients with metal-on-metal implants. There are differences between blood and serum, but blood will give the total circulating metal concentration, although both can be used.

<u>Nutritional assessment</u>. For the assessment of deficiency, please note the special sampling precautions that need to be taken. The considerable doubt regarding nutritional requirements for chromium, and the variable concentration of contaminating chromium in TPN fluids, suggest that regular monitoring of serum chromium in patients receiving long term TPN is desirable. Supplementation should be adjusted accordingly.

<u>Occupational exposure</u>. Occupational exposure is monitored by measuring urinary excretion of chromium with results corrected for creatinine content of the urine.

References

Anderson RA. Chromium metabolism and its role in disease processes in man. Clin Physiol Biochem 1986; 4: 31-41

Angerer J, Amin W, Heinrich-Ramm R, Szadkowski D, Lehnert G. Occupational exposure to metals. 1. Chromium exposure of stainless steel welders – biological monitoring. Int Arch Occup Environ Health 1987; 59: 503-12

Hannemann F, Hartman A, Schmitt J, Lützner J, Seidler A, Campbell P, Delaunay CP, Drexler H, Ettema HB, Garcia-Cimbrelo E, Huberti H, Knahr K, Kunze J, Langton DJ, Lauer W, Learmonth I, Lohmann CH, Morlock M, Wimmer MA, Zagra L, Günther KP. European multidisciplinary consensus on the use and monitoring of metal-on-metal bearings for total hip replacement and hip resurfacing. Orthop & Traumatology: Surgery & Research 2013; 99: 263-271.

Hart AJ, Sabah S, Henckel J, Lewis A, Cobb J, Sampson, B, Mitchell A, Skinner. JA, The painful

metal-on-metal hip resurfacing. J Bone Joint Surg [Br] 2009;91-B:738-44.

Medicines and Healthcare Products Regulatory Agency. Medical Device Alert. All metal-on-metal (MoM) hip replacements (MDA/2010/033). London: MHRA, 2010

Mertz W. Chromium in human nutrition: a review. J Nutr 1993; 123: 626-33

Sampson B, Hart AJ. Clinical usefulness of blood metal measurements to asses the failure of metal-onmetal orthopaedic implants. Ann Clin Biochem 2012; 49: 118–131.

Sidaginamale RP, Joyce TJ, Lord JK, Jefferson R, Blain PG, Nargol AVF, Langton DJ. Blood metal ion testing is an effective screening tool to identify poorly performing metal-on- metal bearing surfaces. Bone Joint Res. 2013; 2: 84-95.