

# Cobalt

Atomic number 27  
Atomic weight 58.93

## Collection

Serum/Plasma	2 mL	Plastic tube No anticoagulant
Urine	20 mL	Sterile Universal

## Reference ranges

			Reference
Serum/plasma	nmol/L	Less than 10	1,2
Blood	nmol/L	Less than 10	3-5
Urine	nmol/L	17	6,7
	nmol/mmol creatinine		
	µmol/mol creatinine	Male 2.0 (95th percentile) Female 2.6 (95th percentile)	7

## References

1. 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.
2. Sampson B. Determination of cobalt in plasma and urine by electrothermal atomisation - atomic absorption spectrometry using palladium matrix modification. *J Anal Atomic Spectrom.* 1988; **3**: 465-469.
3. 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
4. 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.
5. 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.
6. 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.
7. 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**

Cobalt is an essential element, being required for the synthesis of vitamin B12. Cobalt metal is used to make high temperature, high strength alloys and for the preparation of tough carbide-tipped cutting and drilling tools. Cobalt alloys are also important for their magnetic properties. Cobalt is also used in the manufacture of semi-conductors, magnetic alloys and catalysts. Cobalt salts are highly coloured and have been used from the earliest times for pigment production. Dicobalt edetate is used in the treatment of cyanide poisoning.

## **Biological function**

The most important role for cobalt is as a component of vitamin B12 or cobalamin. This is produced by bacteria and is an essential nutrient. There are several cobalamin dependant enzymes. Cobalt is also essential for a few other enzymes. One mammalian cobalt containing enzyme is methionine aminopeptidase 2.

## **Deficiency**

Vitamin B12 – cobalamin – contains cobalt and deficiency of this vitamin, causing pernicious anaemia, is due to failure of absorption from the diet through absence of the so-called intrinsic factor.

Cobalt deficiency per se is virtually unknown in man, although occurring in animals: an anaemia results from the inability of microorganisms in the gut of the affected animals to manufacture sufficient quantities of vitamin B12.

## **Toxicity**

Inorganic cobalt causes increased production of haemoglobin and can induce hypertriglyceridaemia and hypercholesterolaemia. Cardiomyopathy has been seen in individuals with chronic ingestion. In the past cobalt has been used as a haematinic agent but this has been discontinued due to possible side effects.

Inhalation of cobalt-containing dust is a hazard in the manufacture and use of hard metal alloy tools, and causes interstitial lung disease with cough and dyspnoea.

Although several other elements such as tungsten, nickel, vanadium and chromium may be involved, this so-called “hard metal” disease is thought to be largely due to the toxic effects of cobalt. Cobalt dermatitis may occur but the condition is more likely from associated chrome or nickel.

## **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 are 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 (118 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.

Cobalt has been implicated in a few rare cases of toxicity seen in these patients, primarily toxicity to sensory nerves, especially aural and visual effects. There has been some evidence that cobalt can cause toxicity in vitro. 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 of Exposure**

For occupational exposure urinary cobalt concentrations provide a sensitive index of recent exposure. Concentrations increase throughout the working day and week but return from very high to basal levels within 2-3 days.

For monitoring wear in orthopaedic implants measurement of serum or blood chromium concentration is the best available index of excess exposure, and concentrations may still be high some weeks after the incident. 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.

### **References:**

Hannemann F, Hartman A, Schmitt J, Lützner J, Seidler A, Campbell P, Delaunay CP, Drexler H, Ettema HB, Garcia-Cimbrello 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.

Lison D, Buchet J-P, Swennen B, Molders J, Lauwerys R. Biological monitoring of workers exposed to cobalt metal, salt, oxides and hard metal dust. *Occup Environm Med* 1994; 51: 447-50

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

Kobayashi M1, Shimizu S. Cobalt proteins. *Eur J Biochem.* 1999 Apr;261(1):1-9.

Sampson B, Hart AJ. Clinical usefulness of blood metal measurements to assess the failure of metal-on-metal 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.

Taylor A. Cobalt Carcinogenesis. In, *Biological Effects of Heavy Metals. Vol II Carcinogenesis*, ed, Foulkes EC. CRC Press, Florida, 1990, pp 159-171