# Copper, Cu (blood and urine)

Copper (Atomic Weight 63.546 ± 0.003 amu) is a metallic element that is an integral part of many metalloenzymes, e.g. cytochrome oxidase, superoxide dismutase and caeruloplasmin. Copper plays an important role in iron metabolism - copper deficiency impairs iron absorption. Deficiency of copper is rare but has been described in patients with severe malabsorption, malnourished infants and individuals on long-term parenteral nutrition or following bariatric surgery[1]. A high intake of zinc can cause copper deficiency by inducing the synthesis of intestinal metallothionein, which chelates copper and prevents its absorption[2]. Serum copper levels are increased in the acute phase response, due to an increase in caeruloplasmin synthesis. Hypercupraemia has been observed in epilepsy[3]. Oestrogens increase serum copper (and caeruloplasmin) concentrations therefore higher levels are seen in pregnancy and those on oral contraceptives[4]. Copper is secreted in bile and can accumulate in blood as a consequence of liver cholestasis. In contrast, cirrhosis may result in low serum copper due to the inability of the damaged liver to synthesise caeruloplasmin. Acute toxicity occurs very rarely and symptoms include nausea, vomiting and dizziness[5].

Serum copper and caeruloplasmin levels are usually low in patients with Wilson's disease and measurement can be requested part of screens for liver dysfunction or in patients with neurologic symptoms. An equivocal test should be followed by analysis of 24hr urine copper. The majority of Wilson's disease patients are diagnosed between the ages of 5 and 35 years, although it has been diagnosed in younger patients and in those their 70s.

Urine copper estimation is useful in the diagnosis and monitoring of Wilson's disease and is a more sensitive and specific test that serum copper/caeruloplasmin for diagnosis of this condition. Patients with Wilson's disease have elevated levels of copper excretion. A penicillamine challenge test increases the sensitivity and specificity by greatly increasing the urinary copper excretion in patients with Wilson's disease.

## General information

**Collection container**

Serum/Plasma (collected into a container shown to be suitable for trace metals)

Adults (internal users): 4.9mL Gel-free Serum (Sarstedt white top)/LiHep Plasma (Sarstedt orange top)

Paediatrics (internal users): 1.2mL Serum (Sarstedt white top)/LiHep Plasma (sarstedt orange top)

External users: separated serum/plasma in a plain plastic tube, which has been shown to be suitable for trace metals

Urine

Plain 24 hour urine container

**Type and volume of sample:**
Serum/Plasma (collected into a container shown to be suitable for trace metals)

Serum (gel-free) or Lithium Heparin. 1.0mL whole blood required (minimum 150L separated serum/plasma)

Urine
Plain 24 hour collection (Random urine samples are unsuitable for analysis)

**Specimen transport/special precautions:**

Internal: No special precautions
External: Separate and aliquot into a secondary tube.

## Laboratory information

**Method principle:**
Inductively Coupled Plasma Mass Spectrometry (ICP-MS), Agilent 7800 series.

**Biological reference range or cut off:**

Serum/Plasma

| | |
|---|---|
| <4 weeks of age | 2-8 µmol/L |
| >4 weeks of age | 13-26 µmol/L |

Urine
<1.0 umol/24h

**Turnaround times:**

| | |
|---|---|
| Serum/plasma | 1 week |
| Urine | 4 weeks |

## Clinical information

**Factors known to significantly affect the results:** Samples collected into EDTA tubes are not suitable for analysis

**Clinical decision points:**

Urine

| | |
|---|---|
| 1.1 to 6.0 µmol/24h | Equivocal (but low probability of Wilson's disease) |
| >6.0 µmol/24h | Supports diagnosis of Wilson's disease |

If post-penicillamine:

| | |
|---|---|
| 12.0 to 25.0 µmol/24h | Equivocal (but low probability of Wilson's disease) |
| >25.0µmol/24h | Supports diagnosis of Wilson's disease |

**References**
1. Griffith DP, Liff D, Ziegler TR, Esper GJ and Winton EF. Aquired Copper Deficiency: A potentially

serious and preventable complication following gastric bypass surgery.
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2. Hoffman HN, Phyliky RL and Flemming CR. Zinc-induced Copper Deficiency. Gastroenterology 1998; 94: 508-12
3. Taylor A. Detection and monitoring of disorders of essential trace elements. Ann Clin Biochem 1996; 33: 486-510
4. Burtis CA, Ashwood ER. Tietz Fundamentals of Clinical Chemistry. 5th Edition. Saunders 2001.
5. Ayling R, Marshall M. Nutrition and laboratory medicine. ACB Venture Publications 2007