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# Biolab Medical Unit

9 Weymouth Street, London W1W 6DB, U.K. Tel: (+44) 020-7636 5959/5905 Fax: (+44) 020-7580-3910  
E-mail: [info@biolab.co.uk](mailto:info@biolab.co.uk) Internet: <http://www.biolab.co.uk>

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## Plasma homocysteine November 2008

### Indications

Homocysteine is a non-essential, thiol-containing amino acid which is produced from the intracellular demethylation of dietary methionine [1]. It is exported from the cells into the extracellular fluid at a slow but consistent rate and circulates in the blood mainly in an oxidised form, bound to plasma proteins. There are two major pathways for its further metabolism – trans-sulphuration to cysteine (by a vitamin B6-dependent pathway) or re-methylation to methionine (by a vitamin B12 and folic acid-dependent pathway). Vitamin B2 is also required for homocysteine metabolism on account of its role in the re-cycling and maintenance of folic acid levels. Excess homocysteine accumulates in the plasma when these pathways are not operating at optimum activity.

While homocystinuria (homocystine in the urine with elevated plasma homocysteine levels) has been known since 1962, the pathological role of moderate hyper-homocysteinemia has only been generally recognised over the past decade [2].

### Patient preparation

Homocysteine is not a component of food or nutritional supplements, so the patient should not fast prior to the test and may continue taking any nutritional supplements as normal. The blood sample of choice should be taken at midday, four hours after a protein-containing breakfast, so as to ensure an adequate methionine challenge (equivalent to about 0.5 gm of methionine).

### Specimen requirements

Synthesis of homocysteine continues in red blood cells *ex-vivo* after blood sampling, unless it is inhibited [3].

Blood should be taken into purple top EDTA tubes containing a special inhibitor (available from Biolab on request). If posted samples must reach Biolab within 48 hours.

### Laboratory Method

High-pressure liquid chromatography. The turn around time for this analysis is 5 working days.

### Interpretation

The reference interval is less than 12.0  $\mu\text{moles/L}$  of plasma homocysteine, but the treatment goal varies (typically less than 7.0  $\mu\text{moles/L}$  of plasma homocysteine). An elevation of the plasma homocysteine by 5.0  $\mu\text{moles/L}$  has been associated with an increase of 1.7 in the odds ratio risk of cardiovascular disease (the same as an increase of 500  $\mu\text{mol/l}$  in plasma cholesterol [4]).

Men, on average, have a slightly higher plasma homocysteine level than women [3]. This is thought to be associated with greater muscle mass, which increases the demand on the labile methyl pool for the synthesis of creatine.

**Price:** The test fee for measurement of plasma homocysteine is £40.00.

## References

1. Finkelstein JD (1990). Methionine metabolism in mammals. *J Nutr Biochem*;5:228-237.
2. Wald DS, Law M, Morris JK (2002). Homocysteine and cardiovascular disease: evidence on causality from a meta-analysis. *BMJ*;325: 1202-1208.
3. Jacobsen DW, Gatautis VJ, Green R et al (1994). Rapid HPLC determination of total homocysteine and other thiols in serum and plasma: sex differences and correlation with cobalamin and folate concentrations in healthy subjects. *Clin Chem* 40:873-881.
4. Boushey CJ, Beresford SA, Omenn GS, Motulsky AG (1995). A quantitative assessment of plasma homocysteine as a risk factor for vascular disease. Probable benefits of increasing folic acid intakes. *JAMA*; 274:1049-1057.