



Glutathione Peroxidase Activity

Our laboratory methods for the measurement of glutathione peroxidase have been updated and improved. Biolab will now report both red cell and plasma glutathione peroxidase activity when red cell glutathione peroxidase is requested. Together with measurement of plasma selenium (which requires a separate test request), this will give an improved picture of the selenium status and antioxidant defences of a broad range of patients, some of whom will have been taking selenium-containing nutritional supplements.

Indications

Glutathione, a tripeptide consisting of glutamic acid - cysteine – glycine, is the substrate for glutathione peroxidase (GSHPx), which protects cytosolic organelles from the damaging effects of the hydroperoxides formed by normal aerobic metabolism. GSHPx catalyses the reduction of hydrogen peroxide to water, with the simultaneous conversion of reduced glutathione to oxidised glutathione [1]. The origin of the formed H_2O_2 is primarily the lipid hydroperoxides which are released from membrane phospholipids by the action of phospholipase A2 during an inflammatory reaction; GSHPx de-toxifies this H_2O_2 by reducing it to water, while at the same time oxidising glutathione. Any deficiency in this de-toxification cycle (e.g. of GSHPx or of glutathione itself) puts the cell at risk from the potentially mutagenic effects of lipid hydroperoxides.

GSHPx thus protects against lower physiological levels of H_2O_2 than does the enzyme catalase, which reduces the higher concentrations of H_2O_2 formed during respiration.

GSHPx contains one residue per mole of selenocysteine, an analogue of cysteine in which selenium is substituted for sulphur. Deficiency of selenium therefore greatly decreases the activity of this enzyme.

Five different isoenzymes of GSHPx are found in mammals [2]:

- a) GPx1; Cellular glutathione peroxidase (cGSHPx, e.g. red cell GSHPx)
- b) GPx2; Gastrointestinal glutathione peroxidase (giGSHPx)
- c) GPx3; Extracellular glutathione peroxidase (eGSHPx, e.g. plasma GSHPx)
- d) GPx4; Phospholipid hydroperoxide glutathione peroxidase (phGSHPx)
- e) GPx5; Epididymis-specific secretory GSHPx

With the exception of phospholipid-hydroperoxide GSH Px (which is a monomer), all of the GSH Px enzymes are tetramers of four identical subunits. Each subunit contains a selenocysteine in the active site which participates directly in the two-electron reduction of the peroxide substrate. The enzyme uses glutathione as the ultimate electron donor to regenerate the reduced form of selenocysteine [3,4], an analogue of cysteine in which selenium is substituted for sulphur. Current concerns about low levels of selenium in the soil in the UK, together with concerns about modern agricultural methods, mean that application of this enzyme measurement may be appropriate in a wide variety of subjects.

P.T.O.

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GSHPx measurement should also be considered in patients who are under oxidative stress for any reason; low activity of this enzyme is one of the early consequences of a disturbance of the pro-oxidant/anti-oxidant balance [5,6,7]. Low activity of GSHPx may be associated with an increase in the incidence of various cancers (especially prostate cancer in the male), and this therefore could be one mechanism for the association between antioxidant depletion and increased cancer risk.

Methodology

The oxidation of glutathione in the presence of glutathione reductase and NADPH, monitoring at 340 nm [8].

Patient preparation

No special patient preparation is needed.

Specimen requirements

Red cells and plasma from heparin blood samples are the sample of choice for GSHPx measurement (tubes available from Biolab on request). If posted, samples must reach us within 24 hours.

Turn around time

1-2 working days.

Interpretation

The Biolab reference interval for GSHPx-I (red cell GSHPx) is now 25 - 50 IU/gm Hb; for GSHPx-3 (plasma glutathione peroxidase) it is 115 - 400 IU/L. Other laboratories may use different reference intervals to interpret their results.

References

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