Superoxide dismutase

Indications

The superoxide radical anion ($O_2^{\bullet-}$) was identified as a normal cellular metabolite in the 1960's. At the same time the enzyme superoxide dismutase (SOD) was identified as the essential component of all aerobic cells. This enzyme catalyzes the dismutation of superoxide into oxygen and hydrogen peroxide:

- Cu^{+2}-SOD + O_2^- → Cu^{+1}-SOD + O_2
- Cu^{+1}-SOD + O_2^- + $2H^+$ → Cu^{+2}-SOD + H_2O_2.

There are at least three forms of superoxide dismutase in nature. Human erythrocytes contain an SOD enzyme with divalent copper and divalent zinc. Human mitochondria (and E. coli) utilize a second form of SOD with trivalent manganese. *E. coli* also has a third form of the enzyme which contains trivalent iron. The Cu-Zn enzyme, which is found in the cytosol of human cells, is a dimer of molecular weight 32,500; the two subunits are joined by a disulfide bond. From its action in de-toxifying superoxide (by dismutation), SOD is an essential component of all aerobic cells.

The radical which SOD detoxifies, superoxide ($O_2^{\bullet-}$), plays a central role in the in-vivo generation of reactive oxygen species (ROS) since it is from this radical that other reactive intermediates appear to derive. $O_2^{\bullet-}$ is generated in mitochondrial respiration, as well as by the enzymes xanthine oxidase and NADPH oxidase. Although most oxygen used in mammalian respiration does not cause tissue damage, the mitochondrion is nevertheless the most important in vivo source of ROS. Mitochondrial $O_2^{\bullet-}$ is produced primarily at complex I (NADH-coenzyme Q) and to a lesser extent at complex II (succinate-coenzyme Q) and complex III (coenzyme QH2-cytochrome C reductases).

Superoxide can, in particular, cause tissue damage by participating in metal-catalyzed pro-oxidation reactions, i.e. the Haber-Weiss reaction, which is a superoxide-assisted Fenton reaction, but its toxicity is limited by the fact that it is a polar molecule and will therefore not cross lipid membranes. De-localised superoxide may be generated in oxidative stress states, including ageing, alcoholism, atherosclerosis, cancer, cataract, cystic fibrosis, diabetes, hepatitis, HIV infection, iron overload, pancreatitis, pre-eclampsia, pulmonary disease, rheumatoid arthritis, and tooth and gum disease. Normally, an early response to oxidative stress is the induction of SOD synthesis and an increase in its tissue activity.

On the other hand, suspected nutritional deficiencies, especially of copper, zinc and manganese, may predispose to poor SOD activity by interfering with the synthesis of the active enzyme.

Synonyms

SOD, SODase, red cell superoxide dismutase.

Patient preparation

No special preparation is required and the patient can continue to take nutritional supplements and medication before the collection of the sample.

P.T.O.

• The Stone House • 9 Weymouth Street • London W1W 6DB England • Tel: (+44) 020 7636 5959/5905 • Fax: (+44) 020 7580 3910 • Email: info@biolab.co.uk •

Specimen requirements
SOD is present in blood as an intracellular component of erythrocytes – together with other antioxidant enzymes. Red cell lysates from heparin or EDTA whole blood are the sample of choice for SOD measurement.

Postal samples must reach Biolab within 24 hours of collection.

Methodology
The xanthine/xanthine oxidase reaction is used to generate superoxide radicals which react with SOD from the patient's erythrocytes; excess, unreacted radicals mix with a tetrazolium salt and the rate of formation of the resulting coloured complex is quantitated spectrophotometrically. The assay is calibrated with known activities of SOD to give a 5-point calibration curve that covers the low, normal and high areas of the reference interval.

This method replaces the previous one used at Biolab.

Turn around time
2-3 working days.

Interpretation

The Biolab reference interval for red cell SOD is 1102 - 1601 international units of activity per gram of haemoglobin. Other laboratories may use different reference intervals to interpret their results.

Low levels of red cell SOD suggest intracellular deficiencies of the SOD enzyme or its co-factors (copper, zinc and manganese); in practice, intracellular copper deficiencies are our most common finding.

High levels of red cell SOD suggest induction of enzyme synthesis in response to oxidative stress.

References

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3. Arthur JR, Boyne R. Superoxide dismutase and glutathione peroxidase activities in neutrophils from selenium deficient and copper deficient cattle. Life Sciences 1985; 36:1569-1575.
4. Chesters JK, Arthur JR. Early biochemical defects caused by dietary trace element deficiencies. Nutrition Research Reviews 1988;1:39-56.

Suggested further reading

Environmental Medicine in Clinical Practice, H Anthony, S Birtwistle, K Eaton & J Maberly. British Society for Allergy, Environmental and Nutritional Medicine Publications, Southampton, UK (Tel: 01703-812124).