

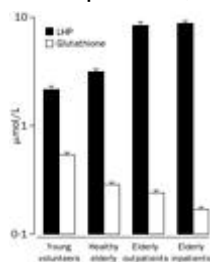
Glutathione: in sickness and in health

S L Nuttall, U Martin, A J Sinclair, M J Kendall

There is increasing evidence that free radical damage may be an important cause of some of the adverse effects of disease and advancing age.¹⁻³ Much of the clinical evidence to support this hypothesis is based on the protective effect sometimes observed in those on diets high in antioxidants and those given antioxidants therapeutically. Further support would be obtained if plasma markers for oxidative damage such as lipid peroxidation products (lipid hydroperoxide [LHP]) were raised and antioxidants such as glutathione were low in the old and the sick, particularly in those who are acutely and severely ill. We have therefore measured plasma glutathione and LHP in healthy young individuals, healthy older individuals, and two groups of elderly patients, one with chronic ill-health attending outpatients and one acutely ill and in hospital.

We studied 66 young healthy volunteers (mean 24· 5 [SD 4· 7] years) and 58 community-based healthy elderly individuals (70· 7 [4· 8] years). Health was defined as an absence of major medical or surgical illness in the previous 5 years, no hospital admissions, no current medication, and a subjective perception of good health. We also studied 49 patients attending general medical clinics (75· 7 [8· 3] years) with a variety of chronic illnesses including ischaemic heart disease, arthritis, diabetes, and hypertension. Finally, 47 hospitalised elderly patients (77· 2 [8· 6] years) were studied during the course of an acute illness within the first week of admission. Non-fasting venous blood was sampled into standard edetic acid (glutathione) and lithium heparin (LHP) tubes. Samples were all taken by one person (SN) and care was taken to minimise haemolysis. They were centrifuged immediately at 3500 rpm, 4°C for 15 min, and plasma stored at -80°C until analysis. Plasma for glutathione was pre-treated with 30% perchloric acid to stabilise thiol groups. Total plasma glutathione was determined by enzyme-rate assay⁴ and plasma LHP by ferrous oxidation of xylenol orange.⁵ A sample size of at least 47 in each group was needed to detect a 20% change in plasma glutathione with 80% power at the 95% confidence limit. Statistical difference between groups was determined by ANOVA and the level of significance taken as $p < 0\cdot 05$.

The results are presented in the figure. The plasma glutathione in young healthy adults was 0· 54 (SE 0· 02) $\mu\text{mol/L}$. In the healthy elderly glutathione was significantly lower (0· 29 [0· 01] $\mu\text{mol/L}$, $p < 0\cdot 0001$). The age-adjusted values for elderly outpatients were significantly lower than in the healthy elderly (0· 24 [0· 01] $\mu\text{mol/L}$, $p < 0\cdot 0001$) and values for elderly inpatients were lower than for elderly outpatients (0· 17 [0· 01] $\mu\text{mol/L}$, $p < 0\cdot 01$). The marker for oxidative damage, LHP, was low in the healthy young adults (2· 14 [0· 17] $\mu\text{mol/L}$) and higher in the healthy elderly (3· 14 [0· 20] $\mu\text{mol/L}$, $p < 0\cdot 01$). It was higher in the sick elderly (8· 51 [0· 66] and 8· 84 [0· 63] $\mu\text{mol/L}$ in outpatients and inpatients, respectively [$p < 0\cdot 0001$ compared with healthy elderly]).



Lipid hydroperoxide and glutathione concentrations in young and elderly healthy volunteers and in elderly patients with chronic or acute illness

Values are mean (SE).

Ageing is therefore associated with a decrease in plasma antioxidants and an increase in evidence of oxidative damage even in those who are apparently healthy. Disease, particularly acute severe disease requiring hospital admission, is associated with greater changes in antioxidants and evidence of oxidative damage. These early observations support the hypothesis that oxidative stress may have an important aetiological role and antioxidants a potential therapeutic role. Further studies are needed to confirm these observations but also to determine which disease processes are most closely associated with oxidative damage.

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 - 3 Fletcher RH, Fletcher SW. Glutathione and ageing: ideas and evidence. *Lancet* 1994; **344**: 1379-80. [\[PubMed\]](#)
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Clinical Pharmacology Section, Department of Medicine, Queen Elizabeth Hospital, Edgbaston, Birmingham B15 2TH, UK (S L Nuttall); and Academic Department of Geriatric Medicine, University of Birmingham, Birmingham

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