

# Oxidative stress or not in healthy older subjects ?

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**Background :** The normal ageing process is thought to be associated with increased oxidative stress (OS). Comparison of the mean blood concentration in OS biomarkers between young and older populations but also correlations between these markers and increasing age tended to support such an idea. However, we have to admit that there is a large number of discrepancies about this matter. In the present work, we propose to evaluate the blood concentration of seventeen OS biomarkers in older (> 65 years) but robust subjects and to compare them with those of normal reference values established in Liège CHU, Belgium (Pincemail et al.. Redox Rep. 2012;17(4):139-44).

**Material and Methods :** Thirty eight older subjects (74 ± 4.2 years) were recruited on the basis of a previous consultation in an ambulatory unit in the Department of Gerontology. Inclusion criteria were age above 65 years and absence of frailty criteria (analysis of frailty according to Edmonton, cognitive performances according to the Montreal Cognitive Assesment, ability to walk without assistive device (Timed Up and Go, Short Physical Performamnce Battery), risk of denutrition evaluated by the short-Mini Nutritional Assesment, autonomy according to Katz and Lawton' scales, risk of depression and comorbidities. The following OS markers were analyzed as previously described by us. Mean (and individual) blood values of these biomarkers were compared to normal reference values established on large populations of healthy subjects (n = 120 to 890) aged between 18 and 60 years (no antioxidant intake, no cardiovascular and cancer antecedents). These values are routinely used in the Clinical Biology Department of the Liège CHU, Belgium.

## Results

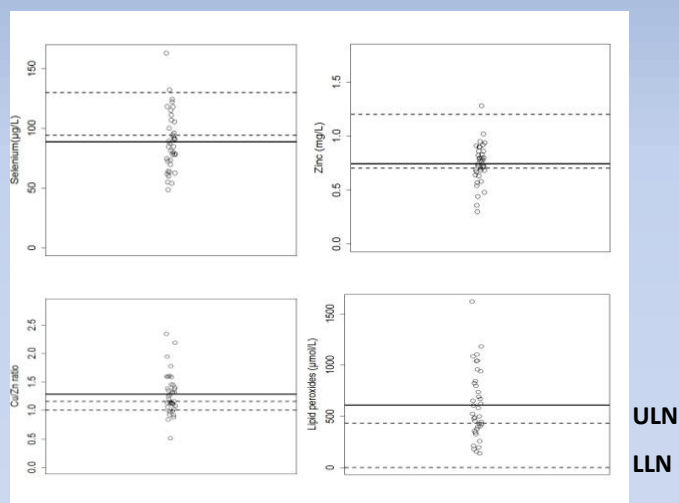
reference

values

n

mean ± SD

parameters	reference values	n	mean ± SD
Vitamin C (µg/L)	6.2 - 18.83	37	10.61 ± 3.29
α-tocopherol (mg/L)	8.6 - 19.24	38	15.10 ± 4.55
γ-tocopherol (mg/L)	0.39 - 2.42	38	1.53 ± 0.60
CoQ10 (mg/L)	0.28 - 1.40	38	0.81 ± 0.27
β-carotene (mg/L)	0.06 - 0.68	38	0.43 ± 0.23
thiol proteins (µmol/L)	310 - 523	38	348.32 ± 49.44
Glutathione (µmol/L)	717 - 1110	38	827 ± 124
Oxidized glutathione (µmol/L)	0.96 - 10	38	3.45 ± 5.88
GPx (UI/g Hb)	20 - 58	38	52.70 ± 11.08
SOD (UI/g Hb)	785 - 1570	38	1641 ± 183
Copper (mg/L)	0.70 - 1.55	38	0.94 ± 0.31
Zinc (mg/L)	0.7 - 1.2	38	0.74 ± 0.18
Cu/Zn ratio	1 - 1.7	38	1.28 ± 0.37
Selenium (µg/L)	94 - 130	38	88.89 ± 25.04
Lipid peroxides (µmol/L)	0 - 432	38	608.11 ± 335.31
Oxidized LDL (U/L)	28 - 70	38	60.61 ± 18.22
Isoprostanes (pg/ml)	152 - 368	40	264 ± 58



Distribution of individual blood values (n = 38) in selenium, zinc, copper/zinc ratio and lipid peroxides. LLN and ULN, lower and upper limit of the normal value obtained in a large normal population (age 18 – 60 years); black solid line, mean value of older but robust adults.

mean values ± DS of OS biomarkers in older but robust adults . Comparison with normal reference values.

**Results and discussion :** The mean blood value of most of the OS markers investigated in older but robust subjects was within the normal reference values. The mean concentration of thiol proteins and zinc was close to the lower limit of the normal values while SOD was above the upper limit of the normal values. The mean blood value in selenium was below the inferior normal value. Both the Cu/Zn ratio and the mean concentration in lipid peroxides were higher than the upper value. Statistical analysis revealed a strong correlation between the Cu/Zn ratio and circulating lipid peroxides (r = 0.72, p < 0.0001). Women exhibited a significant higher mean value in lipid peroxides than men (808 +/-340 µM vs 407 µM +/-174 µM, p < 0.0001), consequently to a higher Cu/Zn ratio (1,45 +/-0.40 vs 1.12 +/-0.24, p = 0.0039).

**In conclusion,** our study raises the question to define which marker or group of associated OS markers must be investigated in order to evidence of not the presence of OS in ageing. The determination of the Cu/Zn ratio which is strongly correlated with lipid peroxides (but not oxidized LDL and isoprostanes) seems to be an interesting and promising marker, more especially in women.

# Oxidative stress and delirium

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Background : Delirium is a common manifestation of brain dysfunction in critically ill patients. According the Diagnostic and Statistical Manual of Mental Disorders(DSM-IV), it is an acute and fluctuant alteration of perception and consciousness due to a somatic serious disorder.

Material and Methods : Data from 15 consecutively admitted intensive care unit (ICU) delirium patients (10 men, 5 women, mean age : 83 ± 4.7 years) were examined to determine whether oxidative stress (OS) existed within 24 hours after admission to ICU. Sixteen markers of OS including antioxidants (vitamin C, alpha and gamma - tocopherol, beta - carotene, thiol proteins, SOD and GPx, ubiquinone, total GSH and oxidized GSH), trace elements (selenium, copper, zinc, copper/zinc ratio) and markers of lipid peroxidation (lipid peroxides, oxidized LDL and isoprostanes) were investigated and compared to those of 38 older but robust adults (19 men and 19 women, mean age : 73 ± 4.2 years) and to normal reference values established in our Liège CHU on healthy population aged 18-60 years (see poster Pincemail et al. Oxidative stress or not in healthy older subjects ?).

## Results

parameters	normal reference value	robust subjects (n = 38)	delirium patients (n = 15)	statistics
CRP (mg/L)	0 - 6	3.62 +/- 5.96	106.14 +/- 137.82	p < 0.0001
interleukine-6 (pg/mL)	ND	2.0 +/- 1.57	45.33 +/- 60.16	p < 0.0001
total cholesterol (mg/dL)	120 - 190	204.68 +/- 35.99	154.33 +/- 51.03	p = 0.0006
vitamin C (µg/L)	6.2 - 18.83	10.61 +/- 3.29	5.92 +/- 2.71	p < 0.0001
alpha - tocopherol (mg/L)	8.6 - 19.24	15.10 +/- 4.55	11.69 +/- 4.05	p = 0.0045
gamma - tocopherol (mg/L)	0.39 - 2.42	1.53 +/- 0.60	0.91 +/- 0.48	p = 0.0008
coenzyme Q10 (mg/L)	0.28 - 1.40	0.81 +/- 0.27	0.56 +/- 0.29	p = 0.004
beta-carotene (mg/L)	0.06 - 0.68	0.43 +/- 0.23	0.38 +/- 0.31	p = 0.23
thiols proteins (µmol/L)	310 - 523	348.32 +/- 49.44	249 +/- 64.20	p < 0.0001
reduced glutathione (µmol/L)	717 - 1110	827.37 +/- 124.31	746.67 +/- 109.33	p = 0.0032
oxidized glutathione (µmol/L)	0.96 - 10	3.45 +/- 5.88	5.26 +/- 11.16	p = 0.48
glutathione peroxidase (UI/g Hgb)	20 - 58	52.70 +/- 11.08	48.40 +/- 9.01	p = 0.19
superoxide dismutase (UI/g Hgb)	785 - 1570	1641 +/- 183	1647 +/- 183	p = 0.99
uric acid (mg/dL)	0 - 7	5.83 +/- 1.56	5.99 +/- 280	p = 0.51
copper (mg/L)	0.70 - 1.55	0.94 +/- 0.31	1.15 +/- 0.27	p < 0.0001
zinc (mg/L)	0.7 - 1.2	0.74 +/- 0.18	0.57 +/- 0.18	p = 0.0035
copper/zinc ratio	1 - 1.17	1.28 +/- 0.37	2.25 +/- 1.03	p < 0.0001
selenium (µg/L)	94 - 130	88.89 +/- 25.04	54.62 +/- 14.91	p < 0.0001
lipid peroxides (µmol/L)	0 - 432	608.11 +/- 335.31	825.80 +/- 428.27	p = 0.055
oxidized LDL (U/L)	28 - 70	60.61 +/- 18.22	52.93 +/- 29.76	p = 0.015
isoprostanes (pg/mL)	ND	41.99 +/- 25.46	32.95 +/- 20;07	p = 0.37

Results and discussion : When compared to older but robust subjects, we observed in our delirium patients a significant decrease of vitamin C by 45%, alpha-tocopherol by 25%, gamma-tocopherol by 40%, ubiquinone by 30%, total glutathione by 10%, thiol proteins by 17%, zinc by 23% and of selenium by 39%. In fact, we evidenced a total and specific collapse of plasma non enzymatic antioxidant defenses since some of these parameters (vitamin C, thiol proteins, zinc and selenium) were largely below the normal reference values. By contrast, there was a significant increase of the copper/zinc ratio by 75% (mean value of 2.25 either two fold the upper normal value) and of lipid peroxides by 35%. Surprisingly both concentrations of oxidized LDL and isoprostanes tended to decrease in delirium patients. Inflammation process present in delirium patients does not seem to be responsible of increased OS (data not shown). In conclusion, delirium is associated with an important increase of OS. This may therefore suggest the implementation of an antioxidant therapy since the admission of delirium patients in ICU.