Concentrations of serum thiols and white blood cell (WBC) count were examined in a group of 124 healthy volunteers. Univariate Pearson’s analysis showed a close correlation between WBC count and total homocysteine and WBC and cysteine.

Several clinical studies have demonstrated that moderately increased levels of plasma total homocysteine (tHcy) are associated with atherosclerosis, cardiovascular disease, stroke and peripheral vascular disease. The mechanism by which homocysteine exerts its effects has not been clearly defined, although it is generally accepted that the accumulation of homocysteine in plasma can damage the endothelium. It has been suggested that homocysteine may induce vascular injury (including endothelial dysfunction, smooth muscle cells proliferation and thiolation of lipoprotein) and affect platelet aggregation and coagulation. Other studies have reported that elevated levels of total cysteine (tCys) are related to an increased risk of cardiovascular diseases and atherosclerosis. Atherosclerosis is a multifactorial disease associated with a variety of risk factors and among them infection and inflammation may contribute to vascular injury and atherogenesis. Inflammation may also promote atherosclerotic plaque rupture and thrombosis. White blood cells (WBC) may serve as an important biomarker for these disease processes. Elevated WBC may also be considered a risk factor for acute myocardial infarction, coronary artery disease and stroke. Although an in vitro association between homocysteine and inflammation has been previously observed, there is little information about the relationship between plasma thiols and WBC count in vivo. We, therefore, measured plasma thiol levels and WBC counts in a sample of patients without evidence of cardiovascular disease in order to verify whether there are any associations between these parameters involved in severe pathological manifestations. We analyzed 124 healthy volunteers, 44 women and 80 men, aged 50±10 years. WBC were measured by a Cell-Dyn 1700 (Abbott) system within 30 minutes from the time the blood sample. Serum thiols were determined by capillary electrophoresis laser-induced detection as described by Zinellu et al. A comprehensive description of the investigated parameters are reported in Table 1. Mean levels of homocysteine and cysteine were about 11 µmol/L (range 5.6–27.5 µmol/L) and 284 µmol/L (range 186.3–406.9 µmol/L), respectively. As might be expected for a healthy population-based sample, 90% of this group had homocysteine levels <15 µmol/L. Since the initial analysis demonstrated that the frequency distribution of tHcy was skewed toward higher values we chose to improve the normality of the distribution by log transformation of all data. Univariate Pearson’s correlation between WBC and serum thiols levels are illustrated in Figure 1. WBC counts showed a significant positive correlation both with tHcy (r=0.25, p<0.005) and tCys (r=0.30, p<0.0005). The association between these thiols and the immune system was also confirmed by our previous data that showed a positive correlation between cysteine and homocysteine levels and neopterin in serum. This molecule was primarily synthesized by human monocytes and macrophages after stimulation by interferon-gamma (IFN-γ) produced by activated helper T-cells. Nevertheless, it is commonly accepted that both cysteine and homocysteine and an activated immune system may contribute to vascular injury and atherogenesis. The biological mechanisms by which homocysteine exerts its noxious effects are still unclear, but it has been found that it stimulates the expression of biologically active monocyte chemoattractant protein-1 (MCP-1) and interleukin-8 (IL-8), two major chemokines for leukocyte trafficking, in human monocytes. Zeng et al. focused on the characterization of the signal transduction pathway(s) mediating the stimulatory effect of homocysteine on both MCP-1 and IL-8 expression in human monocytes. These investigations indicated that oxidative stress had a determinant role in the stimulatory effect of homocysteine most likely via activation of the redox-sensitive transcription factor NF-kB. Homocysteine-induced B lymphocyte proliferation is mediated by oxygen radicals such as O₂, OH⁻ and H₂O₂, generated...
The ability of oral vita-
tin K to correct the INR in patients who are discontinuing warfarin was the target range in over-antico-
gulated patients suggests that it might be useful to nor-
malize the INR in the peri-operative setting. Administer-
ing a small dose of oral vitamin K 24 to 48 hours prior to the procedure may shorten the time period during which patients are not receiving warfarin thus obviating the need for bridging therapy. Before such a treatment strat-
A randomized, blinded study in 30 patients was undertaken. This study found that low dose oral vita-
m K was more effective than placebo when used to correct the INR in patients who are discontinuing warfarin. Larger studies will be required to determine if the use of oral vitamin K, for example in patients who are temporarily discontinuing warfarin to under-
go interventional procedures, is safe and effective.

Thrombosis

**Oral vitamin K produces a normal INR within 24 hours of its administration in most patients discontinuing warfarin**

A randomized, blinded study in 30 patients was undertaken. This study found that low dose oral vitamin K was more effective than placebo when used to correct the INR in patients who are discontinuing warfarin. Larger studies will be required to determine if the use of oral vitamin K, for example in patients who are temporarily discontinuing warfarin to undergo interventional procedures, is safe and effective.

**References**

2. Jakubowski H, Metabolism of homocysteine thiocysteine in human cell cultures. Possible mechanism for pathological con-
3. Jacob N, Bruckert E, Giral P, Foglietti MJ, Turpin G. Cysteine and homocysteine le vels after the log transf ormation of pro-inflammatory and pro-atherosclerotic responses. WBC increment, thus promoting or contributing to the
l and interleukin-6 in human monocytes. Circ Res 2005;95:311-
20.
9. Heinecke JW, Rosen H, Suzuki LA, Chair A. The role of sulfur-
containing amino acids in superoxide production and modifica-

**Figure 1.** Univariate Pearson’s correlation between WBC count and
cysteine and homocysteine levels after the log transformation of all data (n=124).

by thiol (-SH) auto-oxidation. Although less reactive than homocysteine, cysteine shares some of the chemical prop-
ties derived from the presence of the sulphydryl group. Cysteine has a general cytotoxicity in vitro and promotes the detachament of human arterial endothelial cells in cul-
ture. It also exhibits auto-oxidation properties in the pres-
ence of metal ions, resulting in the generation of free rad-
cicals and hydrogen peroxide that promote the activation of the cellular immune system by enhanced induction of NF-κB and MCP-1. Finally cysteine can suppor-
t the activation of the cellular immune system by enhanced induction of NF-κB and MCP-1. Finally cysteine can suppor-
t the activation of the cellular immune system by enhanced induction of NF-κB and MCP-1. Finally cysteine can suppor-

**Ciraco Carru,* Luca Deiana,* Salvatore Sotgia,*
Maria Franca Usai,* Angelo Zinellu**

*Chair of Clinical Biochemistry, University of Sassari; Italy

Correspondence: Dr. Ciraco Carru, MD, Chair of Clinical
Biochemistry, University of Sassari, viale San Pietro 43/B, 07100
Sassari, Italy. Fax: international +39.079.228120.
E-mail: carru@uniss.it

**haematologica/the hematology journal | 2005; 90(1) | 137 |**