ASSOCIATIONS OF THE PLASMA INTERLEUKIN 6 (IL-6) LEVELS WITH DISABILITY AND MORTALITY IN THE ELDERLY IN THE TREVISSO LONGEVA (TRELONG) STUDY


*ARGel, Interdisciplinary Geriatric Research Association, Trento Trieste Aven. 19, I-31100 Treviso, "Department of Statistics University of Padova, Via Cesare Battisti, 241, I-35121 Padova, "Clinical Chemistry Laboratory Regional Hospital Treviso, Piazza Ospedale, 1, I-31100 Treviso, "Transfusional Center, Regional Hospital Treviso, Piazza Ospedale, 1, I-31100 Treviso, "Mario Negri Institute for Pharmacological Research, Via Eritrea, 62, I-20157 Milano, Italy

*Corresponding author:
Phone/Fax: +(39-0422)-231-791; E-mail: m_gallucci@tin.it

SUMMARY
IL-6 expression is regulated by the interplay of several transcriptional and hormonal factors, including sex steroids and glucocorticoids. In late life IL-6 expression increases as a result from loss of the normally inhibiting sex steroids. IL-6 is one of several proinflammatory cytokines. It has been proposed that many chronic inflammatory diseases are the result of a dysregulation of IL-6 expression. In this work we demonstrate that increased IL-6 levels in elderly are associated with higher disability and mortality, also independently of age and comorbidity.

Keywords: Interleukin-6; disability of elderly; mortality; comorbidity in elderly

INTRODUCTION
IL-6 is a pleiotropic cytokine produced by many different types of cells including immune and also many non-immune cells and organs (Bethin et al., 2000; Path et al., 2001). The biological functions of IL-6 include the regulation of proliferation, differentiation and activity of a wide variety of cell types (Ershler and Keller, 2000) and participation in neuro-endocrine and immune system homeostasis (Bethin et al., 2000). IL-6 plays a role in acute-phase reactions, in the balancing of the pro-inflammatory/anti-inflammatory pathways and in the stress response (Xing et al., 1998).

An age-related increase of IL-6 concentration has been found in serum, plasma and supernatants of mononuclear blood cell cultures from elderly people and centenarians (Ershler and Keller, 2000). Some population-based studies would identify the magnitude of IL-6 serum level as a reliable marker for functional disability and as a predictor mortality
among elderly (Cohen et al., 1997; Ferrucci et al., 1999; Harris et al., 1999; Volpato et al., 2001). The aim of this study was to verify mutual relations between IL-6 serum level, disability and mortality in a sample of elderly people over the age of 70 years, living in Treviso. This study is part of the "TREVIso LONGEVA" (TRELONG) Targeted Health Research Project, supported by the Veneto Region, Treviso Municipality and Province, Cassamarca Foundation and other organizations. ARGel, Interdisciplinary Geriatric Research Association, collected the data consisting of biological, medical, social, economic, demographic and quality of life data in 670 elderly 70 years old and over in the city of Treviso, a representative city of North-East of Italy (Gallucci, 2002, 2004; Gallucci et al., 2007).

SUBJECTS AND METHODS

The population over the age of seventy living in the municipality of Treviso was divided according to sex and age into eight groups (with four age groups: 70-79, 80-89, 90-99, 100 and over) within which a predetermined number of individuals was extracted, 250, 200, 200 persons respectively, half male and half female and all those aged 100 and over. Systematic sampling within each of the 6 layers related to the population under 100 years of age. The sample, involving a total of 670 people, might be weighted then with reference to the population distribution. Data were collected through an interview and a blood sample. The interview was administered at subject’s home by interviewers who were trained and standardized on interview taking, as well as conducting tests and clinical examination.

Blood samples were drawn at the patient’s home by nurses. Samples of 30 ml of peripheral blood were collected at home for each subject. Blood samples were transported to the clinical chemistry laboratory of Treviso Hospital, within 30 minutes. Same aliquots of blood were at once used for routine hematological and clinical chemistry tests performed by using standard methods to evaluate the general health status of the subjects. Other blood aliquots were processed in the same laboratory to collect serum and plasma (tubes containing anticoagulant NaEDTA) and to isolate blood leukocytes for the biobank of Transfusional Center Unit. For this purpose the blood was centrifuged at 1500 g for 10 min at 40°C. Then the plasma and serum were separated and stored at -80°C in 500 μl aliquots. IL-6 plasma level (Keller et al., 1996; Ershler and Keller, 2000) was quantified by ELISA kit (Ultra Sensitive ELISA kit, BioSource, USA). The minimum detectable amount was 0.10 pg/ml.