

## **METHADONE AND BUPRENORPHINE MAINTENANCE EFFECTS ON IMMUNE SYSTEM FUNCTION: COMPARISON WITH UNTREATED HEROIN ADDICTS**

Somains Lorenzo<sup>1</sup>, Franchi Silvia<sup>2</sup>, Leccese Vincenzo<sup>1</sup>, Gerra Gilberto<sup>3</sup>, Panerai Alberto E<sup>2</sup>, Sacerdote Paola<sup>2</sup>

<sup>1</sup> Addiction Treatment Centre, Health Local Unit ASL 12 Biella

<sup>2</sup> Department of Pharmacology, via Vanvitelli 32, 20129 Milano

<sup>3</sup> Health Local Unit AUSL Parma

Opioids, especially heroin and morphine, produce severe changes of the immune system, affecting both cellular and humoral immunity and altering resistance to a variety of infectious agents. Studies of drug abuse with heroin have shown that this opioid attenuates the immune response, and might be a cofactor in the pathogenesis of HIV or HCV infection. It has been suggested that that long-term methadone treatment can restore the immune function. The potent partial agonist buprenorphine is increasingly used for drug abuser treatment due to its favourable pharmacodynamic properties; moreover preclinical studies indicate that buprenorphine possesses a safe immunopharmacological profile. For these reasons, we studied the immune function of 3 group of subjects: group A comprised 9 subjects addicted to heroin and that use sporadically other drugs or alcohol; group B was composed of 12 patients who had been addicted to heroin, in treatment with methadone (30-130 mg) since at least 6 months; group C comprised 12 patients who had been addicted to heroin, in treatment with buprenorphine (2-16 mg) since at least 6 months. A group of sex and age matched healthy controls was also studied.

Blood samples added with EDTA were collected in the morning and peripheral blood mononuclear cells (PBMC) obtained by gradient centrifugation on Ficoll Paque. Phytoemagglutinin (PHA)-induced lymphoproliferation and the production of the T helper (Th)-1 cytokine IL-2 and of the Th2 cytokine IL-4 by cultured PBL was evaluated.

PHA-lymphoproliferation in group A was lower in comparison with controls as well as methadone and buprenorphine treated subjects. In contrast, a good level of proliferation was evident in methadone and buprenorphine treated patients. It is well known that a balanced Th1/Th2 response is necessary for a correct homeostasis of the immune system. In our study we observed a dysregulation of this balance in heroin addicted subjects, while the Th1/Th2 system appeared to be well conserved in the methadone and buprenorphine treated groups.

In conclusion we can suggest that the immune abnormalities that are observed in heroin addicted subjects can be restored to almost normal values by controlled treatment with methadone and buprenorphine. Although changes in life habits may have contributed to immune system normalization, buprenorphine and methadone immuno-neutral properties appears primarily implicated in restoring immune system functions.