

## REGENERATIVE MEDICINE IN SPINAL CORD INJURY. REQUIREMENTS AND PITFALLS

Alfredo Gorio<sup>1,2</sup>, Giovanni Marfia<sup>1</sup>, Laura Madaschi<sup>1</sup>, Daniele Bottai<sup>1,2</sup>, Anna Maria Di Giulio<sup>1</sup>

1) Pharmacological Laboratories, Dept. of Medicine, Surgery and Dentistry, Università degli Studi di Milano; 2) Clinical Pharmacology, IRCCS Humanitas, Rozzano; Milano

Accounts of spinal cord injuries and their treatment date back to ancient times, even though there was little chance of recovery from such a devastating injury. The earliest is found in an Egyptian papyrus roll manuscript written in approximately 1700 B.C. that describes two spinal cord injuries involving fracture or dislocation of the neck vertebrae accompanied by paralysis. The description of each was "an ailment not to be treated." Most injuries to the spinal cord don't completely sever it. Instead, an injury is more likely to cause fractures and compression of the vertebrae, which then crush and destroy the *axons*, extensions of nerve cells that carry signals up and down the spinal cord between the brain and the rest of the body. An injury to the spinal cord can damage a few, many, or almost all of these axons. Regeneration or replacement of dead or damaged cells is the primary goal of regenerative medicine and one of the prime motivations for studying stem cells. It is thus of significant interest that I.V. administered adult neural stem cells are incorporated into the lesioned cord and produce therapeutic benefit by modifying the environment of the damaged area. For studies like this, it is important to strictly correlate the therapeutic effect with the presence and the identification of live grafted cells at the site of injury, and exclude the possibility of cell fusion or phagocytosis by macrophages. This must be done by grafting other type of cells, and, in addition, explanting the cells from the injury back in culture and conducting karyotyping. A procedure should be included for eliminating the graft after behavioural recovery occurs, to show that the graft is or is not required for the improved outcome. It cannot be ascribed to administered stem cells any recovery of structure and function, when live grafted cells cannot be firmly traced at the site of neurodegeneration with the methods summarized above. Following the early isolation of adult neural stem cells, several possible brain sources have identified and different neuronal degenerative conditions have been studied so far. Many questions related to their application, however, still remain unanswered. Another important issue for the clinical application is the identification of a human source sufficient for the need, here we report that a possible supply may be represented by post mortem explants of brain tissue.