In vitro **effects of cobalt ions on CNS derived cell lines**

Several neurological symptoms associated with the toxic action of cobalt ions have been reported among patients with metal-on-metal (MoM) hip prostheses made of cobalt-chromium (CoCr) alloy. The sporadic nature of these manifestations, combined with the fact that the medical evidence is relatively new, have contributed to poor understanding of the impact of cobalt poisoning on the brain. In the present study, we characterise the cytotoxicity of cobalt ions in human U-373 astrocytoma and SH-SY5Y neuroblastoma cell lines. Metal ion uptake with different cobalt chloride concentrations (0 to 500μM) for three time-points (24, 48 and 72h) was measured using inductively coupled plasma mass spectrometry (ICP-MS), while cell viability was tested with MTT and Neutral Red (NR) assays, and by microscopy.

The results show that cobalt uptake is dose and time-dependent (up to 415.23, and 69.47μg/L for astrocytes and neurons, respectively), which corresponds with the significant decrease in cell viability ($p<.05$) at high cobalt concentrations both for the MTT and NR assays. IC50 values were 438.27±37.73 and 267.36±14.57μM at 48h for astrocytes and neurons, respectively (similar values for 72h), with the MTT assay more sensitive at detecting toxicity, suggesting involvement of redox mechanisms. Morphological changes, such as extensive vacuolization of the cytosol, usually associated with autophagy, were observed in the course of cell death. These results indicate that exposure to cobalt at high concentrations could have deleterious effects on brain cells. Future focus will be on the mechanism(s) responsible for cobalt uptake, which may provide a therapeutic intervention for MoM patients.