Plenary Session I (cont.)

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NEUROPROTECTION AND DEVELOPMENT IN EXTREMELY PREMATURE LAMBS SUPPORTED ON THE EXTRACORPOREAL ENVIRONMENT FOR NEONATAL DEVELOPMENT (EXTEND) DEVICE

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Purpose: We have developed an EXTracorporeal Environment for Neonatal Development (EXTEND) device that provides physiologic support to extremely premature lamb fetuses for up to 28 days. Support of normal neurologic development is a critical requirement for clinical translation. We hypothesized that EXTEND would provide neuroprotection from hypoxic injury and support normal neurodevelopment and maturation.

Methods: Seven premature fetal lambs (gestational age 112±4 days) were maintained on EXTEND for up to 28 days (mean 23±5 days). Fetal growth was monitored by ultrasonography, including bi-parietal diameter for assessment of brain growth. Upon post-mortem analysis, brain weight and degree of structural maturation was assessed and compared to six age-matched control lambs. Histology was reviewed independently by two neuropathologists blinded to treatment group. Luxol fast blue staining for regional myelination was quantified using Aperio ImageScope software. Iba-1, a marker for microglial activation and inflammation, was also assessed. Statistical comparisons were made via Student's t-tests; data are presented as mean ± SD.

Results: Bi-parietal diameter in experimental animals followed a normal growth rate and the brain:body weight ratio was not different from control animals (1.28±0.1% vs 1.26±0.4%, $p = 0.92$). Cerebral and cerebellar cortical neuronal layers were preserved in experimental animals. There was no histological evidence of ischemic injury and there were no significant differences in corticospinal and capsular myelination ($p>0.08$ for all regions tested) or Iba-1 positivity ($p=0.3$) compared to controls.

Conclusions: Lambs delivered prematurely and maintained on our extracorporeal support environment display evidence of normal brain growth and maturation, without signs of hypoxic or ischemic injury. This system has the potential to prevent much of the neurologically associated morbidity and mortality due to extreme prematurity in humans.