

The effect of recurrent hypoxia-reperfusion on lipid peroxidation in the fetal lamb brain: a path analysis

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Objective: To determine the effects of variable recurrent oxidative stress on lipid peroxidation in the fetal brain:

Experimental Design: Acute, partially exteriorised fetal lamb with intermittent total cord occlusion.

Setting: The Vivarium of Westmead Hospital, University of Sydney, and The Chinese University of Hong Kong.

Methods: 32 fetal lambs were exposed to graded hypoxia, induced by intermittent total umbilical cord compression of 30 second, 60 second and 90-second duration, occurring every minutes for a total of 27 occlusions over 81 minutes. Three sham experiments were also performed. A causal model for oxidative stress was defined: occlusions leading to hypoxia with a rise in hypoxanthine; reperfusion during intervals between occlusions leading to the accelerated production of xanthine and uric acid and the generation of oxygen free radicals, which in turn, are responsible for the rise in lipid peroxidation. Path analysis was performed to assess the strength of the relationships between these variables and the cord occlusion length, the interval between occlusions and the duration of the experiment.

Results: Sham experiments showed no change in OHP production. Following 30-second umbilical cord occlusions a 6-fold drop in mean OHP was observed between carotid arterial and jugular venous levels. In contrast, following occlusions of 60 seconds (or longer) duration a median 20-fold increase in OHP production was observed. The path analysis supported the causal model as originally defined.

Conclusions: Peroxidation of lipids in the brain occurs under conditions of severe hypoxia/reperfusion associated with intermittent umbilical cord occlusions of 60 seconds or longer.