Dr. E. Neil Gunby - AFRRI

A portion of the research effort at the Armed Forces Radiobiology Research Institute has been directed toward the development of a reproducible animal model of head injury which would allow assessment of biomechanical, physiological, clinical and pathologic changes associated with traumatic unconsciousness. This model is based on the production of unconsciousness in the Cynomolgus monkey using angular acceleration to stimulate a "controlled whiplash".

Briefly a nitrogen powered, hydraulically damped shock test device (Bendix Hyge Shock Tester) is mounted horizontally and a linkage and helmet assembly is attached. Physiologic sensors are implanted to monitor blood pressure, pulse, electrocardiogram, respiration, and visual and somatosensory cortical evoked responses. The head is then secured in the helmet assembly with a LEXAN face mask and ear bars and dental stone is poured into the remaining space so that the head and the helmet will be accelerated and decelerated as a single unit. The linkage allows rotation through a 30°, 45° or 60° arc with variation of the center of rotation from the brainstem to the upper thorax.

When preparation and positioning have been completed, several sets of physiologic data are collected in real time with a Digital Equipment Corporation PDP 11/70 computer to establish baseline values. At this time clinical observations of reflexes and level of consciousness are also made. In this way each subject serves as its own control.

Then a ten millisecond acceleration-deceleration pulse occurs. The level may be varied up to 2,000 g's and is monitored by a uniaxial accelerometer (Entran Devices) mounted on the helmut cap and by two high speed cameras (Red Lake Industries) filming at 4,000 frames per second. These films confirm displacement and the fact that head and helmet move as a rigid assembly.

Immediately following this event clinical and physiologic data collection is resumed and continues until the animal has recovered to pre-acceleration status or until a stable state of unconsciousness is obtained without indication of improvement (a minimum of one hour post-acceleration). When this is accomplished, the animal is removed from the helmut and a perfusion in vivo is done with Karnofsky's solution.

Evans Blue Solution tagged to albumin is injected prior to acceleration to provide a marker for cerebral edema.

Afterward correlation of the loss of cortical evoked responses and their recovery is compared with the clinical assessment of the duration of unconsciousness. These factors are then compared with pathologic observations. Results within each group, i.e., center of rotation or arc, may then be compared.

In addition to these studies with a live animal model, a small series of experiments with animal cadavers has been completed. The preparation is similar except that the anesthetized animal is exsanguinated and blood volume is replaced with heparized saline through femoral arterial and venous catheters using a pusatile perfusion pump (Havard Apparatus Co.). When venous return indicates complete exsanguination, the cadaver is refrigerated for periods of time ranging from 24 to 72 hours. The cadaver is then prepared for acceleration as in live experiments except that physiologic sensors are omitted. The cadaver is perfused with heparized saline and Evans Blue Dye tagged to albumin marker through femoral artery catheter before and during acceleration. Afterwards formalin perfusion is performed and a pathologic evaluation follows.

Based on our small series of cadaver animals, there appears to be a marked difference in pathology seen in the cadaver animals and live animals subjected to the <u>same</u> biomechanical input. While the photographs of the gross pathology illustrate this well, several general observations summarize these differences. First, in the cadaver animals, there is evidence of cerebral edema in the flattening of the cerebral gyri. There is less extravasion of Evans Blue and the edema is more generalized. The live animals in contrast show discrete lesions with localized hemorrhage correlating with Evans Blue extravasion. Finally, the cadavers refrigerated for longer periods showed impaired perfusion and vascular collapse (at 96 hours).

Conclusions:

1. Based on limited findings to date, the pathologic changes in live and cadaver animals indicate there is an apparent disruption of

the blood-brain barrier after death probably due to autolysis that produces significant brain edema and alteration in the pathologic findings in cadavers up to 48 hours.

2. In cadavers over more than 48 hours as compared to live subjects, there is some resolution of edema but there is also an apparent vascular collapse which inhibits good perfusion at the time of acceleration and thus distorts pathology.

3. Cadaver models may therefore be a misleading substitute in head injury experiments.