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Artifacts Encountered in Cadaver Vascular Pressurization Experiments

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Work conducted in the laboratory of Alan Nahum, M.D., at the University of California at San Diego, utilizes pressurization of cadaver intracranial vasculature as an integral part of the experimental protocol. Our rationale for this procedure is as follows:

(a) Severe clinical brain injury is predominately demonstrable as injury to the brain vasculature as documented by autopsies, operative findings and results of cranial diagnostic studies (angiograms, brain scans, computerized cranial tomography).

(b) Although there is no doubt that brain parenchyma in the cadaver is altered from the living state, the nonliving brain vasculature maintains its integrity when challanged by certain substances (india ink solution) while losing integrity to other (iodinated contrast agents).

(c) Thus, by pressurization of cadaver cerebral vasculature with solutions that contain a visible marker, such as india ink, injury to that vasculature can be detected by extra-vascular extravasation of the marker.

We encountered two types of artifact utilizing this approach and this forms the substance of this brief report.

Our standard protocol calls for dissection of the carotid and vertebral arteries in the neck, their cannulation after ligation of the external

carotid artery, and perfusion first with warm physiologic saline followed by saline containing india ink. A good flow of india ink-saline from the jugular veins suggests adequate perfusion. The perfusion pump delivers the solution in a pulsatile manner with peak pressures in the 120 mm/Hg range.

When perfusion is good, the brain takes on a bluish-gray hue and methyl salicylate cleared blocks of brain tissue show the india ink solution confined intravascularly in vessels small enough to be arterioles, possibly capillaries. We do not see spontaneous rupture of vessels using this protocol except in the case of previous cerebral vascular accident. In such instances, even when the cerebral infarct is of a chronic nature, i.e. changes in the gross examination of the infarct area suggest month to years since the actual infarct, the india ink marker extravasates in the area of the infarct. This artifact can be misleading if the presence of the infarct is not detected since the extravasation of marker may be interpreted as evidence of acute vascular injury when the cadaver is subjected to significant cranial loading.

We call attention to this artifact to point out that cadavers whose medical history contains information suggesting acute or chronic stroke should probably be excluded from use in cerebral vascular pressurization experiments.

Our second artifactual problem was encountered when we made adjustments in our protocol to improve the degree of vascular perfusion. The problem here revolved around our inconsistent success in actually perfusing all

of the distal cerebral vasculature, particularly the terminal branches of the vertebral-basilar system. Our difficulty was presumed to be caused by preferential perfusion of one area of distal run off so that perfusate pumped into both carotids and vertebrals would tend to flow into the middle cerebral artery distribution because of the anastomotic nature of the circle of Willis and the lower resistance run off effect that seems to be an attribute of the middle cerebral circulation.

We attempted to approach this problem by perfusion of the cerebral vasculature in vitro utilizing direct cannulation of the carotid and vertebral arteries at the base of the brain following removal of the brain. Using this technique, hemostats can be placed across the circle of Willis to force perfusion into each major branch of the cerebral vasculature and thereby improve perfusion of the anterior cerebral arteries and the vertebral-basilar system.

We realized that perfusion of these systems after cerebral loading would not be as near physiologic as adequate perfusion during the loading process, but we hoped that vascular injury might well occur in a nonperfused vessel that would be detected by post-loading in vitro perfusion.

We chose a peak perfusion pressure of 120 mm/Hg and utilizing the in vitro method post-loading we began finding small brain stem vascular ruptures in a distribution consistent with human autopsy material from severe lethal head injury.

Our excitement was short lived, however, when we ran controls. In material that had not been loaded, similar brain stem vascular injuries

were seen. This suggests to us that *in vitro* perfusion is likely to produce artifactual vascular damage, at least at the perfusion pressure we employed.

This raises the question as to why we did not see artifactual brain stem vascular rupture in controls utilizing the *in vivo* neck dissection approach to cerebral perfusion. This is probably due to the pressure drop from cervical carotid/vertebral artery to the intracranial extension of these vessels. We have measured the pressure in the cadaver carotid siphon while perfusing the carotid in the neck at 100 mm/Hg and have found the siphon pressure to be 70 mm/Hg. One might anticipate a further drop by the time perfusate reaches the cerebral arteries, particularly the basilar artery, and may explain our failure to detect brain stem artifact using the *in vivo* technique.