Although optimizing myocardial outcome is an intuitive focus for patients undergoing cardiac surgery, it became apparent from the early days of cardiac surgery that improving overall perioperative outcome was as much dependent on non-cardiac, as cardiac outcomes. The brain is a particularly susceptible organ to injury in this operative setting. Whether neurologic injury presents as overtly as stroke or fatal coma, or as subtle as mild cognitive impairment, the full spectrum of brain injury plays a substantial role in determining the success of the overall cardiac operation. A successful (and life-saving) operation on the heart becomes moot if accompanied by a devastating neurologic injury. Although it is clear that brain injury, in some form, occurs in a widely variable subset of patients after cardiac surgery, the precise mechanisms by which this injury occurs remains incompletely understood. It is likely that the etiology is multi-factorial, with the relative contribution of the various injury mechanisms, be they related to embolic phenomenon or other ischemia mediated processes (further superimposed on a profound inflammatory response), being unclear. [1] Furthermore, with increasing evidence that subtle brain injury can occur in settings other than cardiac surgery it suggests that inherent patient factors may be as important as the direct contributions of the cardiac surgical procedure itself. [2,3]

Major theories have been proposed regarding the etiology of brain injury center upon cerebral microembolization of both particulate and gaseous material,[4-6] global hypoperfusion of the brain (global cerebral hypoperfusion) [7], inflammation (both systemically and within the brain itself),[8,9] temperature perturbations [specifically the occurrence of hyperthermia either during rewarming from cardiopulmonary bypass (CPB) or spontaneous hyperthermia in the post-bypass period], [10,11] cerebral edema (and possible related blood brain barrier dysfunction), [12] as well as the influences of genetics on both the susceptibility to injury or the inability to repair from injury once it has occurred. [13,14] Insights have also been gained from the identification of the occurrence of cognitive decline in off-pump cardiac surgical settings [2] as well as non-cardiac surgery itself. [3] Although we (as anesthesiologists) may have some reluctance to admit it, the drugs we use may also contribute to this problem. For example, evidence is emerging that some of the anesthetics themselves can induce long-term brain dysfunction in animals. [15]

Without doubt, tens of thousands (if not millions) of emboli are generated during CPB many of which finding their way to the cerebral vasculature. [16] Sources for these emboli are numerous and include those generated de novo from the interactions of blood within the CPB apparatus, those generated within the body by the release of atheromatous material or entrainment of air from the operative field, and those added to the CPB apparatus exogenously such as by debris that can be added by the cardiotomy suction or even though injections into the venous reservoir of the CPB apparatus itself. [17-22]

There are several now classic publications outlining the relationship between emboli and cognitive decline after cardiac surgery. However, one of the major limitations in understanding this relationship has been the relative inability to discern between gaseous and
particulate microemboli. No widely available equipment (Doppler or otherwise) can reliably discern between the two types. In addition, the estimates of cerebral embolic load have likely been grossly inaccurate by the selective nature of monitoring only certain (usually middle cerebral arteries) cerebral vessels. Typically, only one and sometimes two major cerebral vessels are monitored with transcranial or carotid Doppler, so in fact usually only one region of the brain is monitored with respect to embolic load. If one looks more generally at some of the histologic analyses that have been done within the brain, by Moody et al., [16] it is likely that there are many millions of cerebral emboli that occur in the brain. However, transcranial Doppler typically picks up embolic numbers in the hundreds to low thousands. One possible explanation for this quantitative discrepancy in transcranial Doppler is that transcranial Doppler signals of emboli are typically over-represented by gaseous emboli due to the nature of the Doppler technology more likely being able to detect gaseous versus other particulate emboli. [23]

One of the other relationships, with respect to the etiology of cognitive decline which has been incompletely understood, is the impact of aortic atheroma to cognition. Where it is widely known (both from non-surgical and cardiac surgical studies) that there is a strong relationship between the presence of aortic atheroma and stroke, the relationship between cognitive outcome and cerebral atheroma is much less uncertain. For instance, there are two studies published that have differing results. [24,25] There is some data that suggests that the more atheroma in the ascending aorta present the more likely there are to be cerebral emboli. [26] However, there is a relative failure demonstrating that these atheroma corresponded to cognitive decline. [24] Part of the discordance between these two findings may be due to the previously outlined innate failure of the Doppler technology to discriminate between gaseous and particulate emboli, thereby misrepresenting the true embolic load.

Irrespective of the variable embolic load that occurs during CPB, there is evidence that hypoperfusion, due to either hemodynamic compromise or the non-pulsatility of bypass leading to ischemia conditions. The support of the theory that global cerebral hypoperfusion during CPB may lead to complications has its origin in the early studies of CPB where systemic hypotension was a relatively common event. Despite this making intuitive sense, that is, that hypotension would lead to global cerebral hypoperfusion, the studies which have examined the relationship between mean arterial pressure and cognitive decline after cardiac surgery have generally failed to show a significant relationship. [27-29] This failure is not mirrored, however, in the setting of cardiac surgery-associated stroke where Hartman et al., [30] and Gold et al., [31] showed that hypotension was associated with worse neurologic outcome in the presence of a diseased aorta. This was not a straightforward relationship, however, and likely represented an interaction between macroembolism and global cerebral hypoperfusion. It is likely, for example, that if one area of the brain which is being fed by a cerebral vessel that is occluded by an atheromatous embolus, it may be susceptible to hypoperfusion (and subsequent ischemia) if the collateral perfusion is decreased by the systemic hypotension. [32] With respect to the interaction with gaseous emboli, it is likely that a higher perfusion pressure may clear the gaseous emboli through the cerebral circulation at a faster rate thus improving cerebral blood flow (CBF) to the area that was previously ischemic.

Supporting the case for global cerebral hypoperfusion has come from some experimental work done by Mutch et al., [7] who looked at magnetic resonance imaging (MRI) scans of CBF which showed progressive decreases during the course of CPB. In continuing to make the case for the significance of global cerebral hypoperfusion, is data demonstrating it may contribute to some of the cognitive decline which has been documented in off-pump CABG (OPCAB)
patients. Extreme hemodynamic instability coupled with cerebral venous engorgement due to Trendelenburg positioning may very well predispose to global cerebral hypoperfusion. Indeed, this has been demonstrated with cerebral oximetry where more cerebral desaturation was seen in OPCAB versus conventional CABG procedures. [33]

Unquestionably, brain injury occurs in the setting of cardiac surgery. Although the precise etiology remains elusive, several advances have been made in our understanding of this problem. However, the work must continue in order to further our understanding of the issue and develop protective strategies. Advancement in pharmacology and non-pharmacologic means of neuroprotection have not yet yielded sufficient positive results to significantly impact this continuing problem.

References:

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