

# Twenty Years Trying to Protect the Brain: What Do We Know?

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**Abstract:** Thirty-five years ago at the Nixon Watergate hearings, a young attorney named Fred Thompson, current US presidential candidate, asked “What did the President know and when did he know it?” A couple of word changes and this question would be appropriate to ask any number of surgical specialties regarding negative neurologic outcomes. Even today, some spe-

cialties are in denial about impaired brain function after surgical intervention. Fortunately, the cardiac surgery community has been in the forefront in efforts to protect the brain. **Keywords:** cardiopulmonary bypass, brain injury, cardiac surgery, neurological protection. *JECT. 2007;39:302–304*

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## INTRODUCTION

The year 1973 (my first year in Houston where I became interested in neurologic outcomes after cardiac surgery) was a time when not dying after heart surgery was considered a very successful operation, and any organ disruption, other than the heart, was accepted as unavoidable. During the next decade, the death rate and overt stroke numbers plummeted as improvements in technology, especially cardiopulmonary bypass (CPB) apparatus, and associated improvements in techniques resulted in improved outcomes.

As better monitoring tools have become available over the past two decades, the etiologic factors associated with brain injury have been identified, and new methods and apparatus have been adopted into practice. Changes in temperature, blood management, new anesthetic and blood gases regimens, different clamps, improved cell savers, ultrasonic aortic evaluations, and changes in CPB technology have resulted in a dramatic improvement in patient outcomes, not only for the brain, but for all organs, despite patients being older and sicker.

The etiologic factors affecting neurologic outcome after CPB are largely known after 20 years of diligent detective work. Armed with new insights regarding how brain function can be impaired during and after surgical intervention, most of the deleterious effects can be avoided by an alert and motivated cardiac surgical team.

## ACUTE SYMPTOMS OF BRAIN INJURY

The first premise is that disrupted brain function may be transient and related to alterations and imbalances in blood chemistry. As equilibrium is restored, so is normal brain function. One must be careful to discriminate between brain lesions and brain impairment. Delirium is characterized by an acute change in cognition and a disturbance of consciousness often associated with a high fever and a generalized systemic inflammatory response syndrome (SIRS).

At Wake Forest University Baptist Medical Center, the low incidence of postoperative delirium seen in coronary artery bypass grafting (CABG) patients has been achieved because of the introduction of the following practices.

1. Keeping our arterial inflow temperatures < 37.5 C, thereby not assaulting the brain structures in the anterior thalamus and hypophysis (pituitary), which control temperature and monitor insulin production, with a hyperthermic insult. It takes between 1 and 2 seconds for blood to travel from the arterial filter to the Circle of Willis, so the temperature of the blood, as it leaves the CPB circuit, is approximately the same as when it perfuses the temperature-regulating system of the brain. It is also not a surprise that blood glucose and insulin levels are in a dynamic state after the pituitary experiences a hyperthermic shock. Consciousness is also affected by rapid changes in both blood sugar and insulin (as in insulin shock), and these same structures are also important in blood chemistry monitoring.
2. Minimizing SIRS is critical for avoiding postoperative

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delirium. We believe that careful blood management, which is best described as preventing blood loss through careful surgical technique and the use of aprotinin, is associated with a decrease in patient temperature fluctuations in the intensive care unit (ICU) and more rapid recovery of a normal sensorium. Minimizing transfusion products is controversial, but there is no question that increased blood product use is correlated with worse outcomes (1). Aprotinin seems to protect the integrity of the endothelium and prevents "leaking," which causes edema. Having a swollen brain (blood-brain barrier breakdown) is not conducive to clear thinking (2,3).

3. Reducing deformable embolic load during CPB. By minimizing blood loss, cardiotomy suction return can be avoided, which is a major source of lipid and gaseous microemboli (MEs) (4,5). The passage of MEs through the cerebrovasculature results in endothelial disruption, brain edema, and cell stress.

### CHRONIC OR LONG TERM BRAIN INJURY

A focal ischemic lesion, an infarct, will cause symptoms within minutes, although the dysfunction may be "silent" to the neurologically unsophisticated and even the patient. Typically it takes about 6 months before the damaged area stabilizes, the edema dissipates, and an assessment of the permanent disability can be estimated. By then, ~90% of the improvement of the initial injury has been realized, and after a year, there is generally no further improvement.

Conversely, the damage caused by microemboli, inflammation, and edema may take quite some time to develop, and the loss of cell mass may not be obvious until several months have passed (3). Assessment of function at this delayed period is problematic because the patient's ongoing vascular disease is contributing to a potential decline in function as well.

If the cardiac team desires to use alterations in brain function to modify their surgical techniques, the best definition of a perioperative brain-related disorder is one that is consistent at 1 week, 1 month, and 6 months (6).

We have recently evaluated our data using this definition and have shown that the number of patients who develop neurologic symptoms 1 month or longer after surgery can be predicted based on age, and this occurs at the same predicted rate that neurologic events would occur in an unoperated population (7). Using the definition of a "persistent" deficit, we find striking differences in patients who had only a single cross-clamp applied (9%) compared with patients who had multiple applications of clamps (26%) (6).

Our experience obtained over 20 years of NIH-funded

research on the topic of brain protection during cardiac surgery can be categorized into three areas.

1. Blood management
  - i. Minimizing bleeding by taking extra care going in "dry."
  - ii. Using aprotinin in a large percentage of the patients where appropriate. Treating suctioned blood from the thoracic surgical field through a continuous autologous cell saver, when possible (5,8).
  - iii. Avoiding suction blood, minimizing the introduction of deformable lipid and gaseous MEs that may initiate SIRS, occlude vessels, and cause brain swelling.
2. Temperature control
  - i. Never exceeding 37.5°C with the arterial inflow blood and care with the addition of any perfusates (because perfusates much cooler than blood temperature may afford the significant possibility of outgassing of gaseous MEs).
  - ii. An embolic occlusion resulting in an infarct at temperatures in excess of 37.5°C will result in a lesion with a 10-fold greater volume than if the occlusion was initiated at 32°C.
3. Aortic manipulation
  - i. The use of a single cross-clamp method, placed after epi-aortic evaluation of the aorta.
  - ii. Avoiding partial occlusion and using a "soft," springy jawed clamp. Hard clamps disrupt the lining of aorta, resulting in a source of continued embolization from clots and necrotic debris in the days immediately after surgery (9).

The surgical team at Wake Forest University Baptist Medical Center, led by Dr John Hammon, have achieved a fivefold improvement in 6-month neurologic outcome over the past two decades by systematically integrating the insights obtained from the research of the CardioNeuro-Protection team. The relationship and interaction between the basic scientists, histologists, radiologist, anesthesiologist, engineer, nurses, and perfusionists have allowed us to make a safe operation even safer.

### REFERENCES

1. Habib RH, Zacharias A, Schwann TA, et al. Role of hemodilutional anemia and transfusion during cardiopulmonary bypass in renal injury after coronary revascularization: Implications on operative outcome. *Crit Care Med*. 2005;33:1749-56.
2. Harris DNF, Bailey SM, Smith PLC, Taylor KM, Oatridge A, Bydder GM. Brain swelling in the first hour after coronary artery bypass surgery. *Lancet*. 1993;342:586-7.
3. Kohn A. Magnetic resonance imaging registration and quantitation of the brain before and after coronary artery bypass surgery. *Ann Thorac Surg*. 2002;73:S363-5.
4. Brooker RF, Brown WR, Moody DM, et al. Cardiomy suction. A

- major source of brain lipid emboli during cardiopulmonary bypass. *Ann Thorac Surg.* 1998;65:1651–5.
5. Stump DA. Embolic factors associated with cardiac surgery. *Semin Cardiothorac Vasc Anesth.* 2005;9:151–2.
  6. Hammon JW, Stump DA, Butterworth JW, et al. Coronary artery bypass grafting with single cross-clamp results in fewer persistent neuropsychological deficits than multiple clamp or off-pump coronary artery bypass grafting. *Ann Thorac Surg.* 2007;84:1174–8.
  7. Leary MC, Saver JL. Annual incidence of first silent stroke in the United States: A preliminary estimate. *Cerebrovasc Dis.* 2003;16:280–5.
  8. Kincaid EH, Jones TJ, Stump DA, et al. Processing scavenged blood with a cell saver reduces cerebral lipid microembolization. *Ann Thorac Surg.* 2000;70:1296–300.
  9. Hammon JW, Stump DA, Butterworth JE, et al. Single crossclamp improves 6-month cognitive outcome in high-risk coronary bypass patients: The effect of reduced aortic manipulation. *J Thorac Cardiovasc Surg.* 2006;131:114–21.